	/		
OECD TG 301C	logKOW=4.88-6.12　　5.17-5.18	100	*Gambusia affinis*
		NOEL 18.2mg/kg/day	42dEC10=0.002 mg/L
OH	BCF	LOEL 8.3mg/kg/day	*Portunus pelagicus*
	BCF=1085-23000	8.3mg/kg/day	40dEC10=0.014 mg/L
4　　41%	BCF=833-4300		
	BCF=577-2258	37.5mg/kg/day	
		81.1mg/kg/day	
		78.7mg/kg/day	
45-467　OH			
277		13　NTP	
65		NOEL 2.4mg/kg/day	
155		24mg/kg/day	
194-		2.4mg/kg/day	
1250		2.4mg/kg/day	
776-		7.2mg/kg/day	
1380			
		24mg/kg/day	
		72mg/kg/day	
187-1550			
194-345			
150　　75%		50mg/kg/day	
50			
6			

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on pentachlorobenzene

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on pentachlorobenzene, on the basis of the draft contained in document UNEP/POPS/POPRC.3/15. The text of the risk profile, as amended, is set out below. It has not been formally edited.

PENTACHLOROBENZENE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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EXECUTIVE SUMMARY

The European Community and its Member States being Parties to the Stockholm Convention have proposed pentachlorobenzene (PeCB) to be listed to the Convention. The Persistent Organic Pollutants Review Committee concluded that PeCB fulfilled the screening criteria set and decided to establish an ad hoc working group to review the proposal further.

Most of the countries who submitted information to the UNEP secretariat reported no production or use of PeCB (Czech Republic, Germany, Lithuania, Mauritius, Turkey, Canada), which is in agreement with the information in the dossier submitted. Past uses of PeCB are PeCB as a component in PCB products, in dyestuff carriers, as a fungicide and a flame retardant and as a chemical intermediate e.g. for the production of quintozene. Major U.S. and European manufacturers of quintozene have changed their manufacturing process to eliminate this use of PeCB. PeCB is also present at low levels as an impurity in several herbicides, pesticides and fungicides. In the United States, some pesticide manufacturers have changed their manufacturing processes to reduce the concentration of HCB impurities in their products, and these changes may have reduced concentrations of PeCB contaminants also. PeCB is also a low level degradation product of some pesticides. Literature sources show that PeCB is of no commercial significance. No trade or stockpiles have been reported.

Nowadays PeCB enters the environment through various sources of which PeCB as a byproduct of incomplete combustion is the largest current source. However, there is considerable uncertainty on the release of PeCB by various sources and available data are limited to the United States and Canada. The limited data available makes it difficult to provide a proper global estimate on amounts and trends. Total estimated annual global emissions of PeCBs based on the US-TRI database were 85.000 kg/yr.

PeCB should be considered as persistent given the estimated and experimental half lives in atmosphere, soils, sediments, and water. According to the available data PeCB has a high bioaccumulation potential. Log Kow values vary between 4.88 and 6.12, with recommended values of 5.17-5.18. BCF values range from 1085 - 23000 L/kg for fish, 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. Due to the fact that biotransformation of PeCB will be insignificant and the substance is very hydrophobic, the compound may also have a high biomagnification potential.
PeCB is moderately toxic to humans and is not classified as a carcinogen. Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms (LC50 for fish, daphnia or algae $\leq$ 1 mg/L). Limited data are available on terrestrial ecotoxicity and data for toxicity to birds are lacking.

Physical and chemical characteristics, such as water solubility, vapour pressure and Henry's Law Constant, are within the range of the other POPs. PeCB can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals. However, estimated half-lives of PeCB in air of 45 to 467 days were reported. Considering its physical and chemical characteristics and persistence in air, PeCB has a potential for long range transport through the atmosphere. This is supported by the presence of PeCB in environmental compartments, including biota, from remote regions.
PeCB is spread widely in the environment on a global scale. Measured levels of PeCB in abiotic and biotic media in remote regions such as the (ant) arctic environment are available, as well as monitoring data on PeCB in abiotic and biotic media of temperate zones. In general, data from developed countries indicates that concentrations of PeCB in the temperate zones of the world seem to decrease. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

Based on the available evidence, PeCB is likely, as result of its long range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

1   Introduction

The European Community and its Member States being Parties to the Stockholm Convention have proposed PeCB to be listed in Annex A, B and/or C to the Convention pursuant to paragraph 1 of Article 8 of the Convention. The complete original proposal is contained in document UNEP/POPS/POPRC.2/INF/5. A summary of the proposal prepared by the Secretariat was provided in document UNEP/POPS/POPRC.2/13.

The acceptance of the original proposal for further consideration by the Persistent Organic Pollutants Review Committee implies that the properties of the substance fulfilled the screening criteria set out in Annex D of the Convention. The next step is to prepare a risk profile for the substance as described in Annex E. This draft risk profile has been prepared following the decision of the Committee, at its second meeting in November 2006, to establish an ad hoc working group to review the proposal further in accordance with the provisions of the Convention (Decision POPRC-2/7).

All data in this document are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (e.g. µg/kg or mL/L).

1.1   Chemical Identity of the proposed substance

1.1.1   Names and registry numbers

PeCB belongs to the group of chlorobenzenes, which are characterised by a benzene ring in which the hydrogen atoms are substituted by one or more chlorines. The chlorobenzenes are neutral, thermally stable compounds with increasing stability and higher melting and boiling points with increasing chlorine substitution. PeCB has a very low solubility in water (Rossberg et al., 2006).

IUPAC Name: benzene, pentachloro-
CAS Chemical Name:
Synonyms: 1,2,3,4,5-pentachlorobenzene; Pentachlorobenzene; PCB; PeCB; QCB; quintochlorobenzene
CAS Registry Number: 608-93-5
EINECS Number: 210-172-0
Trade names: -

1.1.2   Structure

1,2,3,4,5-Pentachlorobenzene
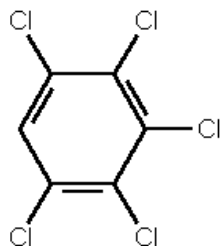
1.1.3   Physico-chemical properties

Mackay et al (2006) provided a recommended value of 0.11 Pa at 20 ^{o}C. Water solubility at 25 ^{o}C varied between 0.135 and 3.46 mg/L, whereas the recommended value in various sources was around 0.55 mg/L. The log Kow values in Mackay et al (2006) varied between 4.88 and 6.12. This source and the PHYSPROP and CHEMFATE databases recommend values of 5.17-5.18 as most reliable. A full listing of the physical and chemical properties of PeCB is listed in Annex II, Table 1.1 in UNEP/POPS/POPRC.3/INF/21.

1.2   Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Pentachlorobenzene

At its second meeting on 6-10 November 2006, the POP Review Committee applied the screening criteria specified in Annex D to the Stockholm Convention, and concluded, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria were fulfilled for PeCB. The Committee decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and observers to submit to the Secretariat the information specified in Annex E of the Convention before 2 February 2007.

1.3   Data sources

Information on the data sources (references and other literature) has been provided in UNEP/POPS/POPRC.3/INF/21 Annex I and III. Where the reviews mentioned above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list. The following parties and observers have answered the request for information specified in Annex E of the Convention: Canada, Czech Republic, Germany, Japan, Lithuania, Mauritius, Switzerland, Turkey, United States of America, International POPs Elimination Network (IPEN), and the International Council of Chemical Associations/World Chlorine Council (ICCA-WCC).

1.4   Status of the chemical under international conventions

PeCB is not included in any international convention. The European Commission has submitted a proposal to include PeCB to the Protocol to the 1979 Convention on Long Range Transboundary Air Pollution (LRTAP) on Persistent Organic Pollutants to the Executive Secretariat of the United Nations Economic Commission for Europe in 2006 (European Commission, 2007). The objective of the LRTAP POPs protocol is to control, reduce or eliminate discharges, emissions and losses of persistent organic pollutants. The UNECE Task Force on POPs identified the following options for possible inclusion of PeCB into the Protocol:
(a) Listing of PeCB in annex I to the Protocol in order to prevent production and use;
(b) Listing of PeCB in annex I and annex III to the Protocol. [ECE/EB.AIR/WG.5/2007/14]

PeCB is identified as a priority substance within the European Water Framework Directive (2000/60/EC). Within the list of these priority substances so-called priority hazardous substances are identified which are of particular concern for the freshwater, coastal and marine environment. These substances will be subject to cessation or phasing out of discharges, emissions and losses within 20 years after adoption of the Directive. The European Commission has proposed to include PeCB as a priority hazardous substance. [COM(2006) 397 final]. PeCB is listed on the OSPAR 1998 List of Candidate Substances (OSPAR, 1998).

2   Summary information relevant for the risk profile

2.1   Sources

Production, use and sources of release have been described extensively in the two documents submitted by Canada (Government of Canada, 1993, 2003), the proposed risk management strategy for PeCB by Canada (Environment Canada, 2005) and the document submitted by the ICCA/WCC (2007). Additional information was retrieved from the documents submitted by other Parties and Observers and from the open literature.

2.1.1.   Production, trade, stockpiles

The submission document for PeCB reported that PeCB was not produced anymore within Europe and North America (Van de Plassche et al., 2002). PeCB has not been reported by EU Industry as an HPVC or LPVC (http://ecb.jrc.it/esis/). Most of the countries who submitted information to the UNEP secretariat reported no production (Canada , Czech Republic, Germany, Lithuania, Mauritius, Turkey, and USA). No intentional production was mentioned in the document submitted by the ICCA/WCC and according to Ullmann's Encyclopedia of Industrial Chemistry PeCB is of no economic significance (Rossberg et al., 2006). No trade or stockpiles have been reported.

2.1.2. Uses

Canada and the USA reported that there is no current domestic commercial demand for PeCB and that PeCB is not used as an end product. Ullmann's Encyclopedia of Industrial Chemistry does not mention any present use of PeCB (Rossberg et al., 2006). However, various past uses or unintentional uses of PeCB are mentioned in the literature:

1. PeCB was a component of a chlorobenzenes mixture used to reduce the viscosity of PCB products employed for heat transfer (Environment Canada, 2005), but new regulations prohibiting new uses of PCB-containing dielectric fluids resulted in a decline of the use of PeCB after 1980. PCBs are still in use in some old electrical equipment in North America and Europe so that there is a small potential for release of PeCB from this source (Environment Canada, 2005). It can be presumed that some PCBs are also still in use elsewhere in the world and some fraction of them contain PeCB. PCBs are being taken out of service in many countries of the world so that any related PeCB emissions are expected to decrease with time.

2. Formerly, PeCB and TeCB could be found in dyestuff carriers. The applications in dye carriers have been discontinued (Environment Canada, 2005). It is not clear from the Canadian document if PeCB, TeCB or both have been used in dyestuff carriers.

3. PeCB can be found as an impurity in several herbicides, pesticides and fungicides currently in use in Canada (Environment Canada, 2005). The US EPA carried out a study to assess the dietary cancer risk of hexachlorobenzene and PeCB as impurities in chlorothalonil, PCNB, picloram, and several other pesticides. PeCB was identified in pentachloronitrobenzene (quintozene), endosulfan, chlorpyrifos-methyl, atrazine, and clopyrilid, but not in simazine, chlorothalonil, picloram and dacthal (US EPA, 1998). Technical grade hexachlorobenzene (HCB) contains about 98 % HCB, 1.8 % pentachlorobenzene and 0.2 % 1,2,4,5-tetrachlorobenzene (WHO-IPCS, 1997). HCB is already listed in annex A and C of the Stockholm convention and it may thus be expected that HCB is of minor importance as a source for PeCB. The present situation for the other pesticides is unknown.

4. The use of PeCB as chemical intermediate is mentioned in WHO-IPCS (1991). So far, only the use as an intermediate in the manufacture of pentachloronitrobenzene (quintozene) has been found in the literature. PeCB is present as an impurity in this fungicide. Van de Plassche et al. (2002) report on the production and use of quintozene in various countries and indicated that the use outside the UNECE region is unknown. Van de Plassche et al. (2002) stated: 'Nowadays, quintozene is manufactured using another production process without PeCB. Amvac does not know of any current quintozene producer using PeCB as feedstock. They conclude that it is unlikely that there are any stockpiles of quintozene containing appreciable quantities of PeCB.' Feiler (2001) in ICCA/WCC (2007) reported that quintozene is now being made by chlorination of nitrobenzene instead of using PeCB as an intermediate. The available data suggest a decrease in PeCB use for the preparation of quintozene. However, this conclusion is based on data for Europe and North America only.

5. PeCB may have been used in the past as a fungicide and as a flame retardant (Van de Plassche et al., 2002). WHO-IPCS (1991) mentions that PeCB was formerly used in a pesticide to combat oyster drills. No further sources of these applications have been found.

6. Less than 0.1 kg per year of pure PeCB was imported into Canada from the United States for use as a laboratory reagent (Government of Canada, 1993). The use as laboratory reagent, based on data applicable to 1995, is also mentioned in Government of Canada (2003). The present situation is unknown.

From the data submitted and data in the literature it is obvious that production and use of PeCB in Europe and North America are negligible. The situation in other parts of the world is less clear.

2.1.3. Releases to the environment

The proposed risk management strategy for PeCB prepared by Environment Canada in 2005 mentions various routes through which PeCB can be released into the Canadian environment (Environment Canada, 2005). The main sources of release in Canada are barrel burning of house-hold waste , wood treatment plants and in service utility poles, pesticide use, dielectric fluid spill and cleanup, municipal solid waste incineration, hazardous waste incineration, magnesium production, solvent use and long range transport. As potential sources of release are mentioned: magnesium production (less than 2% of total annual releases), chlorinated solvents (negligible), secondary copper and aluminium processing (no data), chemical manufacturing (unlikely), iron and steel mills (scarcity of data), petroleum refineries (unlikely), wastewater treatment plants

(unlikely), textile mills (unlikely), long range transport (amount not known, expected to decrease) (Table 2.1, Annex II, UNEP/POPS/POPRC.3/INF/21).

The sources of release and potential sources are described more extensively in Environment Canada (2005). The total release provided by Environment Canada in the risk management strategy of PeCB (Environment Canada, 2005), 41.9 kg/yr, is a factor of 10 lower than the release of >580 kg/yr provided in the Priority substances list assessment report for PeCB (Government of Canada, 1993), submitted by Canada for the drafting of this Risk profile. The most significant sources in the Canadian risk management report (Environment Canada, 2005), barrel burning of household waste (21,93 kg/yr), municipal solid waste incineration (2.36 kg/yr), hazardous waste incineration (1.84 kg/yr) and magnesium production (1.53 kg/yr), were not identified as sources in 1993.

Data on releases of PeCB in the USA can be found in the U. S. EPA Toxics Release Inventory (TRI) (US EPA 2007a, http://www.epa.gov/tri/tridata/index.htm#pdr). The TRI contain release data for 2000 – 2004. Total releases vary between 1512 and 763 kg PeCB/yr and include air emissions, surface water discharges, underground injection, on site releases to land and transfers off-site to disposal. Air emissions between 2000 and 2004 were 74, 34, 37, 40 and 100 kg/yr respectively. Water emissions are in the same order of magnitude (See Table 2.2, Annex II, UNEP/POPS/POPRC.3/INF/21). The US also indicated in their comments that the data provided by TRI on "on-and-off-site releases" include amounts that would not be released to the environment because they were subject to treatment or other management activities. The TRI data does not cover all the industry sectors, which implies that total releases in the US can be much higher than those provided. Release data from other countries are not yet available.

The ICCA/WCC provided a document with an estimation of the annual global emissions of PeCB based on the U. S. Toxics Release Inventory (TRI) (ICCA/WCC, 2007). PeCB formation has been observed during combustion of municipal solid waste. The reported emission factors varied primarily due to differences in combustion conditions rather than fuel composition or waste content. The combustion of PVC may be a source of PeCB formation (Kim et al., 2004; Aracil et al., 2005; Muller et al., 1997), but the relative importance of this source is debated. There are other processes which produce a variety of chlorinated aromatics that may contribute to PeCB even if PeCB has not been explicitly detected and reported yet. Total estimated annual global emissions of PeCBs by ICCA/WCC (2007) were 85.000 kg/yr, about 2000 times the amount estimated for Canada and 850 times the total release of the United States. Most of the emission sources are similar with those provided in the Canadian risk management document (Environment Canada, 2005), but some are different. Hazardous waste incineration and wood treatment plants are lacking in the ICCA/WCC study, whereas combustion of coal and combustion of biomass, which amounts half of the total global emissions, are lacking in the Canadian study. Other PeCB sources could include quintozene degradation, titanium dioxide production, and ore treatment for the production of metals including magnesium, copper, niobium, and tantalum (ICCA/WCC 2007 citing Beck and Hansen, 1974; Knutzen and Oehme, 1989; Doering et al., 1992, and Vogelgesang 1986). No quantitative estimates are provided, because there is no quantitative information on which to base them. Although chemical manufacturing was thought to be unlikely as a source, the highest reported chlorobenzene concentrations in Canadian sediment have been observed near industrial sites (Government of Canada, 2003).

In conclusion, PeCB can enter the environment through various sources of which PeCB as a byproduct of incomplete combustion is the most significant current source. Nearly all fuels contain some chloride, especially biomass and waste. In industrial chlorination reactions it is possible that PeCB is produced as a byproduct and it probably accounts for some of the emissions reported. For a number of potential sources, such as copper and aluminum processing plants and steel mills no or limited data are available. From the data provided in the various documents one may expect a decrease of releases through past intentional use, due to phasing out of PeCB. In the case of unintentional releases as a byproduct of combustion a decrease can be expected in those cases where measures were taken to reduce the releases of other byproducts/emissions. The global estimate should be considered taking into account these uncertainties and the variation in industrial and waste handling processes among the various countries.

2.2   Environmental fate

2.2.1   Persistence

Pentachlorobenzene (PeCB) can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals (CEPA, 1993). There are no experimental data on atmospheric degradation, but the estimated half-life of PeCB is 45 to 467 days. For PeCB, the calculated half-life in air based on reaction with OH-radicals is 277 days (EPISUITE, US EPA, 2007b). Vulykh et al. (2005) estimate a half-life in air of 65 days based on modelling data. This estimate is the

result of degradation as well as dry and wet deposition and gaseous exchange with various surfaces. The atmospheric half-life of PeCB due to the degradation process only is estimated to be 155 days.

In the OECD TG 301C test PeCB was non-biodegradable (NITE, 2007). Photodegradation of PeCB is fast in surface water under sunlight irradiation: 41% loss after 24 hours (HSDB, February 2000). The half-life of PeCB in surface water was estimated to range from 194 to 1250 days, the estimated half-life for the anaerobic biodegradation in deeper water ranged from 776 to 1380 days (CEPA, 1993).

Wang et al. (1994) studied PeCB in spiked (4.5 µg/kg) and sewage sludge-amended soil (3 µg/kg) at 20-30 °C. Half of the dosage of PeCB is lost rapidly by volatilization, followed by degradation with half-lives of 187 days (spiked soil; 1.4 o.m.) to 1550 days (amended soil, 4.5% o.m.). Formation of bound residues is a relatively minor route of dissipation on soil. Scheunert et al. (1985) recovered 1% of a 2 mg/kg dosage as bound residue after 126 days. Under aerobic conditions PeCB is persistent in soil.

Beck and Hansen (1974) found disappearance half-lives based on duplicate samples, of 194 – 345 days in an aerobic loamy sand soil (1.9% o.m.); 18-20°C) treated at 7 mg/kg. Standard deviations were 20 to 25%. The 95% confidence limits are thus 112-726 and 289-3176 days. Since the values were based on duplicates, the total range of 112-3176 days represents the experimental results. Soils were kept in 10L buckets covered with two plastic sheets. During the experiment that lasted 600 days, water losses were compensated; apparently the total water content of the soil evaporated from the soils every 100 days (Bro-Rasmussen et al., 1970). The reported disappearance values are based on log(2)/k; instead of ln(2)/k. Correct half lives thus span the range of 260 – 7300 days. The contribution of volatilization of PeCB to these half lives is unknown.

Susarla et al. (1997) investigated the degradation of HCB in a methanogenic slurry of sandy sediment (<1% o.m.) with lake water (1:3 v/v), spiked at 1.14 mg/L. After 75% of the HCB had degraded after 150 days, the degradation of the primary metabolite PeCB followed first order kinetics with a half life of approximately 50 days at 25 °C. Masunaga et al. (1996) investigated the degradation of PeCB in sulfidogenic estuarine sediments that had been pre-exposed to various chemicals from local industries. Sediment slurries contained 272 g/kg solids; of which 12% can be lost by ignition, and were kept at 25°C. PeCB half-life was 18 days. In autoclaved samples the half-life was 990 days.

In sediment cores of Ketelmeer in The Netherlands, that had been selectively enriched with HCB to get a dechlorinating anaerobic community, PeCB is not persistent: the adapted anaerobic microflora gives half-lives of about 6 days at 25 °C when spiked at 50 µg/L (Beurskens et al., 1994). A mixture of clay loam soil (5.38% o.m.) and a sterile medium (50 g soil and 70 ml medium) was incubated anaerobically at room temperature after inoculation with a 10% slurry of an adapted microbial culture. The soil was spiked with 14.2 mg/L HCB, 25 mg/L PeCB, and 254.1 mg/L 1,2,4-TCB. Concentrations of PeCB decreased with a half-life of approximately 23 days. Chlorobenzene accumulated as the major metabolite after 80 and 142 days to 1 mmol/L (Ramanand et al., 1993). So far, only one bacterial strain which reductively dechlorinates chlorobenzenes has been isolated (Adrian and Görisch, 2002).

Comparison of PeCB concentrations in Ketelmeer sediment (The Netherlands) sampled and measured in 1972 to concentrations in samples taken in 1988 from sediment layers deposited around 1970, showed a small but statistically significant decline of 35%. HCB had decreased by 80%. Lower chlorinated benzenes like di- and tetrachlorinated benzenes had increased up to 80% (Beurskens et al., 1993). Lake Ketelmeer sediment contains 9-13% o.m. (Aarnoutse et al., 1996; Cornelissen and Gustafsson, 2004). In a UK soil (Woburn) that had received 25 separate sewage sludge applications in 20 years time (until 1961), approximately 21% of the added PeCB was still in the soil 30 years after application had stopped (Wang et al., 1995). This soil received about 25% of its dry weight in sludge. Assuming that sludge contained 80% organic matter and a 2% organic matter breakdown per year, the mean o.m. content was 15%. Input of HCB during these years was about 4 times higher than the PeCB input; and HCB residues also declined to 22% in these 30 years.

Experimental data on degradation of PeCB in water are lacking. PeCB is expected to dissipate from the water phase to the sediment or into the air. PeCB is persistent in soils and sediments under aerobic conditions. In anaerobic sediment-water slurries PeCB is considered persistent, except at temperatures above 10°C in combination with low organic matter contents. Higher organic matter contents seem to drastically increase the persistency. Actual field measurements of PeCB may overestimate persistency as a result of formation of PeCB from HCB. The true field half life of PeCB is estimated around 6 years in organic soil and sediment in the temperate zone.

PeCB should be considered as persistent given the magnitude of estimated and experimental half-lives in atmosphere, soils, sediments, and water. Persistence in the environment depends on the rate of photo-oxidation, the presence of oxygen and organic matter.

2.2.2   Bioaccumulation

PeCB is highly hydrophobic. Mackay et al. (2006) report log K_{ow} values between 4.88 and 6.12, with recommended values of 5.17-5.18. Therefore, it can be assumed that the compound has a high bioaccumulation potential. This is confirmed by the data shown in Table 2.3, Annex II, UNEP/POPS/POPRC.3/INF/21 which summarizes values considered reliable according to the Klimisch criteria (Klimisch, 1997).

BCFs range from 1085 - 23000 L/kg for fish; 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. It should be noted that for the lowest BCF data for fish it is not explicitly clear if exposure concentrations have been measured (Schuler et al., 2007). If these BCFs are based on nominal instead of measured exposure concentrations, then they are probably lower than the 'real' BCFs based on measured concentrations.

In conclusion, these values show that PeCB can be considered to have a high bioaccumulation potential. Due to the high $logK_{ow}$ and the fact that biotransformation may be insignificant (Schuler et al., 2006, 2007), the compound may also have a biomagnification potential. However, data on the biomagnification of PeCB are lacking.

2.2.3   Potential for Long range environmental transport

Overall persistence and long-range transport potential were estimated for five new POP candidates (including PeCB) with the OECD Pov & LRTP Screening Tool using the input properties in the POPRC proposal documents (Wegmann et al, 2007). The tool does not provide absolute levels in the environment, but facilitates comparison with earlier identified POP substances. The authors conclude that, although there are considerable uncertainties in the chemical characteristics of the five chemicals investigated, the POP candidates (including PeCB) have Pov and LRTP properties similar to those of several earlier identified POPs.

There is also evidence for long range transport of PeCB based on calculations of the transport distance of PeCB through the atmosphere. Mantseva et al. (2004) developed a multi-compartment transport model for the evaluation of long-range atmospheric transport and deposition of POPs. Based on this model assessment a transport distance in Europe of over 8 000 km is calculated for PeCB. The model is described in detail by Vulykh et al. (2005) who assessed a transport distance of 8 256 km. Based on measured concentrations in air samples of North America an empirical estimation of 13 338 km was made for the long rang transport of PeCB through air (Shen et al., 2005). This distance is larger than that of the other organochlorine pesticides that were part of this study including the currently listed POPs dieldrin, DDT and heptachlor.

Monitoring data also indicate that PeCB is subject to long range transport. PeCB was detected in air and precipitation at various locations in the world, many of those far from its sources. In all air samples collected in 2000-2001 at the 40 sampling stations in North America (including 5 arctic stations), PeCB was detected. The measured concentrations were relatively constant across the continent, averaging 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). According to the authors, the small spatial variability across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global atmosphere. The presence of PeCB has been reported in several abiotic (air, rainwater, water, sediment and soil) and biotic (fishes, birds, mammals) matrices at remote regions including the arctic region and Antarctica. These are described in detail in the section Exposure.

In conclusion, modeling, monitoring data of PeCB in air, as well as PeCB's chemical properties indicate that this substance has a considerable potential for long range environmental transport. The presence of PeCB in matrices from remote regions, some that can only have received PeCB after transport via air, supports the conclusion that PeCB is subject to long range transport.

2.3   Exposure

PeCB is spread widely in the global environment. The first two sections will focus on the levels of PeCB in abiotic and biotic media in remote regions such as the (ant)arctic environment. The third section will focus on monitoring data on PeCB in abiotic and biotic media of temperate zones, as well as observed trends. The last section discusses human exposure.

2.3.1   Levels in abiotic environmental matrices of remote regions

Atmospheric concentrations of PeCB have been measured at various locations around the world. Concentrations in air collected at Alert (Northwest Territories, Canada) ranged from 0.0031 to 0.135 ng/m^3 (Government of Canada, 1993). Measured concentrations across North America averaged 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). They also observed that atmospheric levels of organochlorine compounds including PeCB increased with increasing elevation in the Canadian Rocky Mountains.

PeCB was found in all water samples collected during a study of the distribution of chlorinated organics in the North Pacific Ocean, the Bering and Chukchi streets (ICCA/WCC 2007 citing Strachan et al., 2001). Concentrations of PeCB in the dissolved phase averaged 0.016 ng/L, while suspended solids represented only a small fraction of the total amount of PeCB. Bottom sediment samples taken from harbours in northern Norway and the Kola Peninsula in the arctic contained PeCB in concentrations ranging from 2 to 5 µg/kg dry weight. PeCB concentrations in four Alaskan arctic lakes sampled from 1991 to 1993 averaged 0.10 ±0.10 µg/kg dry weight (ICCA/WCC, 2007 citing Allen-Gil et al., 1997). Concentrations in soil samples from the coastal areas of Victoria Land (Antarctica) varied between 0.4 and 1.3 µg/kg dry weight (Borghini et al., 2005). In these soil samples PeCB was the dominant organic compound. Muir et al. (1995 as cited by ICCA/WCC, 2007) reported PeCB in sediment of a series of remote lakes in northern Canada. Sediment surface layer concentrations (representing a period of time estimated between 1979-1988) of PeCB in these northern lake ranged from less than 0.01 to 0.73 µg/kg sediment.

2.3.2.   Levels in biota of remote regions

Contamination of the environment and biota in remote regions can be a threat to vulnerable species and ecosystems. PeCB is detected in mosses, fish, penguin eggs, seals and predatory mammals in the arctic and antarctic regions.

PeCB concentrations in mosses from coastal areas of Victoria Land (Antarctica) varied between 1 and 2.4 µg/kg dry weight (Borghini et al., 2005). The mosses do not have a root system and their supply is largely dependent on atmospheric deposition. The measured PeCB concentrations in both mosses were higher than those of the currently listed POPs HCB and DDT that were also included in this study. PeCB concentrations in mosses growing in the Andean Mountains at elevations between 700-4500 m ranged from 0.2 – 2.4 µg/kg dw (Grimalt et al., 2004). This study shows that PeCB is likely subject to cold-trapping. An inverse relationship was established with higher PeCB concentrations at lower temperatures. A similar relationship was established for mountain soils in Tenerife (Ribes et al., 2002).

Concentrations (µg/kg wet weight) of PeCB in organs from fish from Alaska and Northwestern Russia and other arctic locations varied between 0.06 ±0.08 and 5.06 µg/kg wet weight PeCB (ICCA/WCC, 2007 citing Allen-Gil et al., 1997, citing Muir et al., 2003, citing Arend et al., 2001, Vorkamp et al., 2004; Corsolini et al., 2006).

In Greenland PeCB was observed at levels of 23 µg/kg lipid weight in ptarmigan liver (1.5 µg/kg wet weight) and 8 µg/kg lipid weight in kittiwake muscle (1.1 µg/kg wet weight) (Vorkamp et al., 2004). Adelie penguin eggs (Antarctic) contained 0.68 µg/kg ww PeCB (Corsolini et al., 2006).

Inuit hunter collected tissue samples of ringed seals from the east and west sides of the Northwater Polnya between Canada and Greenland during the spring of 1998 (ICCA/WCC, 2007 citing Fisk et al., 2002). The concentration (wet weight) of PeCB in these sampled ranged from 7.3 ±1.9 µg/kg in male ringed seals to 8.4 ±1.1 µg/kg in females from the west side. Seals from the east side (Quebec) contained 5.0 ±0.5 µg/kg (males) and 7.0 ±1.5 µg/kg (females). Seals from the White Sea in Northwestern Russia collected in the period 1992-1998 contained PeCB at concentrations ranging from 0.9 (bearded seal) to 12.0 µg/kg lipid weight (harp seal) in their blubber (ICCA/WCC, 2007 citing Muir et al., 2003). The mean concentration (± standard deviation of the 10 samples) of PeCB in 1992 was 11±2.0 ng/g lipid weight whereas the concentration of PeCB in 1998 was 5.0±1.8 ng/g lipid weight. PeCB concentrations in bowhead whales collected between 1994 and 1998 averaged at 0.3 ± 0.1 and 0.8 ± 0.1 µg/kg wet weight in liver and blubber, respectively (ICCA/WCC, 2007 citing Hoekstra et al., 2002). St. Lawrence Bay (Canada) Beluga Whale blubber was found to contain 24.5 (1.56 – 1510) µg/kg (lipid weight) PeCB for females and 144.5 (1.5 - 1500) µg/kg for males (ICCA/WCC, 2007 citing Hobbs et al., 2003). In Greenland, blubber of musk ox (captured between 1998 and 2001) was reported to contain 0.32 µg/kg lipid weight PeCB (equivalent to 0.29 µg/kg ww) (Vorkamp et al., 2004).

PeCB has also been detected in polar bears. The compound was present in all 15 fat and plasma samples taken from polar bears from the arctic Svalbard islands (Gabrielsen et al., 2004) at an average concentration of 7.9 and a maximum of

13.9 µg/kg (wet weight). Similar concentrations are observed in polar bears from Alaska, Canada and East-Greenland, according to the authors. Concentrations and body burdens of chlorobenzenes (including PeCB) in polar bears of different ages have been studied before and after their seasonal fasts (ICCA/WCC, 2007 citing Polischuk et al., 2002). The authors conclude that no PeCB is metabolized or excreted during the fast, leading to increasing concentrations of the compound in fat tissue. Amounts of PeCB in cubs is reported to be greater than in adults due to the fact that nursing bear cubs receive an increased amount of PeCB.

The accumulation of PeCB has also been measured in the arctic fox during 1999-2001 (ICCA/WCC 2007, citing Hoekstra et al., 2003). The animals were collected some distance from human habitation to minimize effects of garbage scavenging. About 20 animals were collected at each site. PeCB concentrations (µg/kg) found in arctic foxes were0.61 ± 0.12 in muscle (Arivat), 0.29 ± 0.06 in muscle (Holman), 0.57 ± 0.11 in liver (Holman), 0.55 ± 0.20 in muscle (Barrow) and 0.73 ± 0.17 in liver (Barrow). Hoydal and Dam (2003) measured concentrations of <0.1 – 37 ng/g wet weight in biota captured in the environment of the Faroe Islands.

King et al (2003) studied the chlorobenzenes spilled after an accident in the Gulf of St Lawrence. There was a rapid decline in tri- to peCB concentrations in snow crabs from sampling location 1 [near the spill] between 1996 and 1998. From 1998 to 2000 the chlorobenzenes concentrations in snow crabs persisted at low levels. In 1996, chlorobenzenes concentrations at locations 2 to 11 were much lower than at location 1, but showed no consistent decrease with time.

2.3.3. Levels at temperate regions including trends

A large quantity of monitoring data exists on PeCB detected in abiotic matrices as well as in biota in temperate zones, mainly originating from developed countries. In general, concentrations of PeCB in the temperate zones of the world seem to decrease. This pattern is representative for that of most POPs. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

A study of the influence of emission sources on atmospheric PeCB concentrations in Germany showed that concentrations were higher at industrial or urban locations (ranging from 0.057 to 0.286 ng/m^3) than at a rural reference site (0.031 ng/m^3) (ICCA/WCC 2007 citing Wenzel et al., 2006). Concentrations at the rural site are comparable to the average atmospheric concentration measured by the Integrated Atmospheric Deposition Network (IADN) above the North American Great Lakes in 2000, i.e., about 0.072 ng/m^3 (ICCA/WCC 2007 citing Buehler et al., 2004)

A clear trend of the presence of PeCB in the environment can be derived from its presence in sediment cores. Sediment cores from the industrially impacted area from Lake Ontario near the mouth of the Niagara River (Canada) show an increase in PeCB concentration from early 1900 until the period 1960-1970 (peak concentration of over 100 µg/kg) after which concentrations declined to about 10% of the peak concentration by 1980 (ICCA/WCC, 2007 citing Durham and Oliver, 1983 and NYDEC, 1998). Also PeCB concentrations in the Niagara river water dropped from 0.351 to 0.093 ng/L during the period 1987-1997 (ICCA/WCC 2007, citing Williams et al., 2000). However, data in the mussel watch programme for the Niagara river do not show a decrease in PeCB concentrations between 1997 and 2000 on several locations (Ministry of the Environment Ontario, 1999, 2003). Concentrations of PeCB in sediment of the Ketelmeer in The Netherlands dropped by 37% in the period 1972-1988 (Beurskens et al., 1993).

PeCB concentrations in Herring Gull eggs from Muggs Island / Leslie spit (Canada) have dropped from 50 µg/kg in 1970 to non-detected at 1 µg/kg in the mid 1990s (ICCA/WCC 2007, citing Bishop et al., 1992; Petit et al., 1994; Pekarik et al., 1998; Jermyn-Gee et al., 2005; Havelka, 2006). Calambokidis et al (1999) studied persistent pollutants in Harbor Seals (Phoca vitulina) in Puget Harbor (US) during the period 1984-1997. They concluded that total TEQ showed a near significant decline by year (p=0.07) and that other pesticides also showed general declining trends. Only for HCB, total chlorobenzenes, and chlordanes was the decline statistically significant. Only recent data (last 15 years) are summarized in Table 2.4 for abiotic and Table 2.5 for biota matrices in Annex II, UNEP/POPS/POPRC.3/INF/21.

During a survey within the Danube Regional Project for the European Water Framework Directive, PeCB was detected in almost all sediment samples at concentration levels of 0.0001 – 3.5 mg/kg and in most of the suspended solid samples at concentration levels of 0.001 – 0.028 mg/kg (Slobodník and Dogterom, 2003). The ATSDR database from the US Government contains 41 records of polluted sites with PeCB. Maximum concentrations of PeCBs at these sites vary between 147 and 5100 mg/kg in sediments and between 0.43 and 2040 mg/kg in soil. Concentrations in fish vary between 0.00019 and 2.4 µg/g (ATSDR, 2007). Neither references mention if these concentrations are based on wet or dry weight basis.

2.3.4. Human exposure

Occupational exposure to PeCB may be through inhalation and dermal contact with this compound at workplaces where PeCB is produced or used. Examples are wood treatment plants, dielectric fluid spill and cleanup, municipal solid waste incinerators, hazardous waste incinerators, and magnesium production plants. Exposure may also arise in occupational settings where the pesticide quintozene is produced and used. The general population may be exposed to PeCB via inhalation of ambient air, ingestion of food and drinking water. Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified (Government of Canada, 1993).

PeCB has been detected in breast milk and found to accumulate in human placenta (Shen et al., 2007). The mean concentration of PeCB in the breast milk of Canadian women taken 3 to 4 weeks after parturition was < 1 μg/kg (trace) with a maximum value of 1 μg/kg. In this survey, the compound was detected in 97% of the 210 samples analyzed (detection limit and sampling period unspecified) (Government of Canada, 1993 citing Mes *et al.,* 1986). In the breast milk of women of Canadian indigenous population, "trace" (< 1 μg/kg) amounts of PeCB were observed in 17% of the 18 samples (detection limit not specified) (Government of Canada, 1993 citing Davies and Mes, 1987). Two other studies investigating PeCB in human milk reported concentrations in the range of 1 to 5 μg/kg (WHO-IPCS, 1991). PeCB has also been measured in abdominal, mammary, and perirenal fat tissue from 27 adult Finnish males and females (Smeds and Saukko, 2001). Workers with occupational exposure to PeCB were found to have higher levels of the substance in blood than control groups (Lunde and Bjorseth, 1977).

2.3.5. Bioavailability

The Environmental Health Criteria on chlorobenzenes (WHO/IPCS, 1991) concluded that limited evidence was available showing that sediment-bound residues of chlorobenzenes are bioavailable to organisms; i.e., aquatic invertebrates can take up residues from sediment, and plants, from soil. Since then, more information on the bioavailability of hydrophobic substances became available.

Bioavailability of chlorobenzenes is inversely proportional to the organic carbon content of the soil or sediment (Government of Canada (2003) citing e.g. van Gestel and Ma, 1988; Hulzebos et al., 1993). It was furthermore stated in the Canadian Follow-up Report that persistent substances can remain bioavailable for long periods of time, thereby increasing the probability and duration of potential exposure relative to compounds that do not persist in the environment.

It is generally accepted that not all fractions of organic pollutants bound on sediments or soils are equally toxic due to their various resistances to desorption. The resistant and sequestered fractions of PeCB are environmentally less harmful than the more readily desorbing, labile, or available fractions. The large fraction of water soluble organic matter in the sediments is potentially highly mobile and could be easily resuspended or leached to the overlying water column. If the soluble organic matter carries the major amount of PeCBs as expected, continuous contamination of the water body from the sediments is very likely. Qiao & Farrell (1996) carried out experiments with PeCB in rainbow trout and concluded that mass balance analysis suggests that the appearance of HCBP and PeCB in the fish after 6 days could not be accounted for solely by the amount of chemical dissolved in the water at the time when the fish were introduced. The chemical uptake in fish with the pharynx plugged, to eliminate the gut uptake route, was similar to that in control fish. Because direct access to bottom sediments did not alter chemical uptake, they concluded that hydrophobic chemicals such as PeCB and HCBP associated with suspended sediments from the Fraser River can readily desorb and be taken up across the gill. Åkerblom (2007) concluded that pesticide sorption to organic particles in standardized toxicity tests is fast and efficient and that substances bound to the sediment may act as a reservoir, continuously supplying the pore water with low pesticide concentrations.

As organic pollutants bound to sediment or organic matter may still become available, an evaluation should focus on sorption and desorption kinetics of PeCB and modifying circumstances rather than on statements on bioavailability. Such data are however scarce.

2.4 Hazard assessment for endpoints of concern

2.4.1. Toxicity

Toxicokinetics

Toxicokinetic studies with rats show that after an oral dose, the substance is distributed to the blood and tissues (Umegaki et al., 1993; ICCA/WCC, 2007 citing Thomas and coauthors). Linder et al., (1980) observed that rats fed with PeCB accumulated approximately 1.5 – 2.2 times the dietary concentration in their adipose tissues. Umegaki et al., (1993) studied the kinetics of PeCB in blood and tissues of rats given a single oral dose by gavage of either 15 mg or 20 mg. PeCB was observed in the blood, liver, kidney, brain, and fat tissue as well as in the feces (4.8% of the dose). In the blood, also the major metabolite pentachlorophenol was observed.

Den Besten et al (1994) studied the urinary metabolite profile of PeCB in the rat after dietary exposure for 13 weeks. PeCB was metabolized to the major metabolites pentachlorophenol (PCP), 2,3,4,5-tetrachlorophenol (TCP), mercaptotetrachloro-phenol (MTCP), the glucuronide derivative of pentachlorothiophenol (PCTP), and the minor metabolites tetrachlorohydroquinone (TCHQ), methylthiotetrachlorophenol (MeTTCP), hydroxytetrachlorophenyl sulphoxide (HTCPS), and bis(methylthio)-trichlorophenol (bis-MeTTriCP). The study also revealed that oxidation of PeCB to 2,3,4,5-TCP was not mediated by cytochrome P450IIIA. In the urine of rabbits exposed to a single oral dose of PeCB, also pentachlorophenol and 2,3,4,5-tetrachlorophenol was observed (Slooff et al., 1991, citing Kohli et al., 1976).

A study with coyotes showed that PeCB is excreted in the faeces (Johnston et al., 1997). Coyotes were dosed with PeCB (single dose of 130, 260 or 520 mg). In both studied matrices, faeces and adipose tissue, residues of PeCB were determined. PeCB was detectable in faeces for six months post-dosing. In the faeces, also the metabolites pentachlorophenol and 2,3,4,5-tetrachlorophenol were detected.

Data on other than the oral exposure route are limited available. WHO-ICPS (1991) indicates that the chlorobenzenes are less readily absorbed through the skin, but that levels of the same isomer of the chlorobenzenes in various tissues appear to be similar, regardless of the route of administration. The ingestion of a lethal dose leads to respiratory paralysis, while the inhalation of high doses causes local irritation and depression of the central nervous system WHO-ICPS (1991).

Acute toxicity

PeCB has been tested on rats and mice. Results of acute toxicity tests are available for oral and dermal exposure (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). LD_{50}s for PeCB (by gavage in peanut oil) are 940 to 1125 mg/kg bw in adult and weanling rats and 1175 and 1370 mg/kg bw in Swiss Webster mice (Linder et al., 1980 cited in Government of Canada, 1993). Decreased activity and tremors were observed in both species at sublethal doses; the kidneys, liver and adrenal glands of rats were also enlarged. In some rats, the gastric mucosa was hyperaemic, and a slight reddish fluorescence of the gastrointestinal tract was observed in both rats and mice under ultraviolet light, suggesting porphyria (Government of Canada, 1993). In the study of Allen et al., (1979, cited in Slooff, 1991), a LD50 of 250 mg/kg bw was observed in rats. Ariyoshi et al., (1975, cited in Slooff, 1991) observed an increase of cytochrome P450 content in rats as well as an increase in the activity of two hepatic enzymes after oral administration of 250 mg/kg bw once daily during 3 days.

To determine a dermal LD50 one concentration (i.e., 2500 mg/kg bw) was tested on rats, but no toxic effects were seen at this dose (Linder et al., 1980 cited in Slooff, 1991). Based on this study, a NOEC of > 2500 mg/kg bw can be established for dermal exposure.

PeCB is classified in the European ESIS database as R22, harmful if swallowed (European Chemicals Bureau, 2007). WHO-IPCS (1991) reported that data on skin and eye irritation potential and on sensitization potential were mainly restricted to 1,2,4-trichlorobenzene. No data were available for PeCB.

Subchronic toxicity

PeCB has been tested on rats and mice. Results of (sub)chronic toxicity tests are available for dietary exposure, see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21. In female Sherman rats ingesting diets containing 500 mg/kg and greater (> 37.5 mg/kg bw/day) PeCB for 100 days, there was an increase in liver weight and hypertrophy of hepatic cells (Linder et al., 1980). There was also an increase in kidney weights and renal hyaline droplet formation in males at exposure levels ≥125 mg/kg (equivalent to ≥8.3 mg/kg bw/day). In addition, at 1 000 mg/kg (equivalent to 81.1 mg/kg bw/day for males and 78.7 mg/kg bw/day for females), the effects observed were: an increase in adrenal weight and focal areas of renal tubular atrophy and interstitial lymphocytic infiltration in males; an increase in kidney weight in females; a decrease in haemoglobin and an increase in white blood cells in both sexes; and decreases in red blood cells and haematocrit in males. The no-observed-effect-level (NOEL) in female rats, derived on the basis of the results of this study, was 250 mg/kg (equivalent to 18.2 mg/kg bw/day); the lowest-observed-effect-level (LOEL) in males was 125 mg/kg (equivalent to 8.3 mg/kg bw/day) (calculations by Government of Canada, 1993).

In a study of NTP (1991) rats and mice were exposed to PeCB through their diet. Observed effects were among others: decreases in the mean body weights of male rats at exposure levels ≥ 1 000 mg/kg diet and in females at all concentrations (≥ 33 mg/kg), increase in absolute and relative liver weights (33 mg/kg in males), centrilobular hepatocellular hypertrophy (as low as 330 mg/kg for males), increases in kidney weights and renal histopathological effects at concentrations as low as 100 mg/kg, nephrotoxic effects in females (≥ 1 000 mg/kg), increase of the concentration of protein in the urine in male and female rats at ≥ 1 000 mg/kg, decrease of free thyroxin and total thyroxin concentrations in male and female rats indicating moderate hypothyroxinemia and abnormalities were observed at concentrations of ≥330 mg/kg in females and ≥ 1 000 mg/kg in males. The incidence of abnormal sperm in males was also increased at both dietary concentrations at which it was examined (330 and 2 000 mg/kg). On the basis of histopathological lesions, the authors considered the NOELs to be 33 mg/kg in male rats and 330 mg/kg in females (approximately 2.4 and 24 mg/kg bw/day, respectively) (calculations by Government of Canada, 1993).

In PeCB exposed mice in the same study NTP (1991), observed effects were among others: ventral swelling and ruffled fur (2 000 mg/kg), increase of kidney weights (≥330 mg/kg in males), functional effects on the thyroid at all concentrations in both sexes (≥33 mg/kg), increase in liver weights (at 100 mg/kg in males). The only exposure-related histological lesion in mice of either sex was centrilobular hepatocellular hypertrophy and minimal necrosis, observed at all concentrations in males and at ≥ 330 mg/kg (equivalent to 68 mg/kg bw/day) in females. On the basis of the histopathological lesions, the authors considered the NOEL in female mice to be 100 mg/kg (approximately 22 mg/kg bw/day). No NOEL for males could be established (LOEL = 33 mg/kg or approximately 5.2 mg/kg bw/day) (calculations by Government of Canada, 1993).

In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

Mutagenicity and carcinogenicity

Epidemiological studies of exposed populations are not available and information on carcinogenicity in experimental animals has not been identified. PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints.

PeCB has been tested negative in the Ames test (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Based on limited available data, mutagenicity in *S. typhimurium* with and without metabolic activation, effects on chromosomes in Chinese Hamster ovary cells *in vitro,* and micronuclei in peripheral blood smears in animals from the NTP sub-chronic study, PeCB has been assessed as not genotoxic (Haworth et al., 1983 and NTP, 1991 cited in Government of Canada, 1993). Several studies (Thomas et al., 1998 and Gustafson et al., 2000; Ying et al., 2001) investigated the tumor-promoting activity in medium term carcinogenicity assays of various chlorobenzene isomers including PeCB. The results suggest that PeCB promotes glutathione *S*-transferase (GSTP1-1) positive preneoplastic foci formation in rat liver, following diethylnitrosamine (DEN) initiation.

Both Health Canada and U.S. EPA have reviewed the cancer toxicity data of PeCB. The cancer weight-of-evidence classification is based on all routes of exposure. Neither group derived a risk value. Both groups concluded that the substance is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC or by the EU (European ESIS database).

Reproductive and developmental toxicity
Available studies concerning the embryotoxicity, foetotoxicity and teratogenicity of PeCB include one study in rats (and one in mice (Villeneuve and Khera, 1975 and Courtney et al., 1977, cited in Government of Canada, 1993) (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Results of the study of Villeneuve and Khera (1975) indicated that PeCB is foetotoxic (an increased incidence of extra ribs and sternal defects was observed in the offspring) at maternal exposure doses of 50 mg/kg bw/day. The exposure concentration was below the concentration that induced toxic effects in the mothers. In mice, no embryotoxic, foetotoxic or teratogenic effects were observed in the offspring at doses which were maternally toxic (50 mg/kg bw/day and above)(Courtney et al., 1977). In the only identified study on reproductive toxicity of PeCB, Linder et al. (1980) reported that suckling pups of PeCB treated mothers fed ≥ 250 mg/kg developed tremors (LOAEL = 18.2 mg/kg/day). At 1000 mg/kg, most sucklings died before weaning.

The studies above are also cited in WHO-ICPS (1991) who conclude that there is some evidence that the higher chlorinated benzenes (TCBs, TeCBs, PeCB) are embryotoxic or fetotoxic at dose levels that are not maternally toxic. WHO-ICPS (1991) also remark that the available data are not consistent and that the toxicities of the various isomers of the TCBs and TeCBs for the mother and fetus vary considerably. Most reported effect (NOAEL, NOEL) and no effect levels (LOAEL, LOEL) vary between 17 and 200 mg/kg PeCB per day.

PeCB showed high oral toxicity with LD50 doses as low as 250 mg/kg bw in rats. From the limited data available, dermal LD50s are higher. Data on skin and eye irritation potential and on sensitization potential are limited. In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg bw per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints. Data on mutagenity and carcinogenity are limited. Both Health Canada and US-EPA concluded that the PeCB is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC, nor by the EU (European ESIS database). There is some evidence that PeCB is embryotoxic or fetotoxic at dose levels that are not maternally toxic.

2.4.2. Ecotoxicity

Aquatic toxicity
Acute and chronic toxicity data are available for both freshwater (see Table 2.7, Annex II, UNEP/POPS/POPRC.3/INF/21) and marine organisms (see Table 2.8, Annex II, UNEP/POPS/POPRC.3/INF/21). The lowest acute toxicity values are 100 µg/L for freshwater fish species (EC50) and 87 µg/L for a marine crustacean (LC50). The lowest chronic values (NOECs) are 2 µg/L for a freshwater fish and 14 µg/L for a marine crustacean. According to these findings, species sensitive to PeCB can be found in both the freshwater and the marine environment.

Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms and which may cause long-term adverse effects in the aquatic environment (Risk phrases N; R50 and R53) (European Chemicals Bureau, 2007). This classification is based on the fact that the substance is very toxic to fish, daphnia or algae (LC50 ≤1 mg/L) and the substance is not readily degradable or bioaccumulative.

Soil and sediment toxicity
Limited data are available for soil and sediment. Tests with various chlorobenzenes were carried out by Van Gestel et al (1991). Two earthworm species were raised on a natural sandy soil (KOBG) and an artificial OECD standard soil. Average LC50 values varied between 115 and 238 mg/kg dry weight, whereas LC50 values in pore water varied between 55.1-117.7 µg/L. Van Gestel et al (1991) concluded that based on pore water concentrations earthworms are more sensitive to PeCB than fish, but that this may be due to differences in test design.

Only one study on the toxicity of PeCB in plants was identified. Duplicate tests were carried out in which *Lactuca sativa* seedlings were grown on OECD soil contaminated with PeCB. The seedlings were harvested after 7 and 14 days. EC50 values varied between 56 and 862 mg/kg dw (Hulzebos et al. 1993). Experiments in solution resulted in an EC50 value of ±1.0 mg/L. Details of the tests are provided in Table 2.9, Annex II, UNEP/POPS/POPRC.3/INF/21.

Toxicity to birds
No toxicity data on birds are available for PeCB.

Multiple chemicals and toxicological interactions
Annex E request information on toxicological interactions involving multiple chemicals (Annex E, b). Limited information is available on this subject. Yoo et al (2003) report on their studies on the kinetics of PeCB: "The kinetics and toxicity of pentachlorobenzene were assessed using a freshwater (*Hyalella azteca*) and marine amphipod (*Leptocheirus plumulosus*). The results of these studies demonstrated the additive toxicity of PeCB with other organic chemicals (pyrene)."

Comparison of exposure and effect data
Several methods, exposure routes and species with very different feeding strategies were used by ICCA/WCC to determine the lethal and critical body burden of PeCB. Based on the general knowledge on substances with a narcotic mode of action and the available data on PeCB, such as the *Hyalella* growth/mortality study and other information discussed, an estimation of 25 mg/kg PeCB/kg (0.1 mmol) was tentatively proposed by ICCA/WCC (2007) as a Critical Body Burden for chronic effects.

A very recent publication of Schuler et al (2007b) has reported critical whole body residues of pentachlorobenzene of 58 mg/kg and 5 mg/kg for *Hyalella azteca* and *Chironomus tentans* respectively. These residue levels are lower than the highest concentrations reported for temperate regions in Table 2.5 in the Annex POPRC3/INF21 and 150-1500 times higher than the highest values of <0.1 – 37 μg/kg wet weight in biota reported for the Faroe Islands by Hoydal and Dam (2003). Other concentrations reported from remote areas are of the same order of maginitude, e.g. Adelie penguin eggs (Antartic) contained 0.68 μg/kg ww (Corsolini et al., 2006) and whole body concentrations from fish in the White Sea were up to 5 μg/kg ww (ICCA/WCC, 2007 citing Muir et al., 2003).

The World Chlorine Council (ICCA/WCC, 2007) has provided information related to two other approaches. The first approach focused on PeCB organic carbon concentrations in sediments from Canadian lakes and showed that in both rural and remote sites, PeCB organic carbon concentrations were 410-75000 times lower than Environment Canada's "estimated no effect value" for freshwater benthic organisms. In the second approach, comparisons were made between exposure estimations for a pisciverous predator and for polar bear using assumptions considered by the WCC as "worst case assumptions", and effect levels derived from human Reference Dose and Tolerable Daily Intakes from USA and Canada. These estimations of exposure were 13 and 20 times lower than the derived effect levels, respectively.

The available information has not been sufficient for confirming if the values given above represent real critical body burdens or just expressions of internal dose or whole body residues levels. Both concepts have fundamental differences related to the understanding of the mechanism of action of the chemical. Nevertheless, it should be noted that expressing the toxicological effects as internal dose or, whenever possible, critical body burdens, improves the effect assessment but only reduces partially its uncertainty. In addition, all the uncertainty related to the exposure assessment remains. While monitoring levels above critical body burdens or internal toxic doses clearly indicate a risk, the fact that current measured concentrations are below these triggers should in no case be interpreted as a confirmation of the absence of risk, particularly in the assessment of POPs and POPs candidates.

3   Synthesis of the information

Pentachlorobenzene is a chlorinated organic compound. According to available data, pentachlorobenzene should be considered as persistent given the considerable number of estimated and experimental half-lives in atmosphere, soils, sediments, and water. Persistence in the environment depends on the rate of photo-oxidation, the presence of oxygen and organic matter. Pentachlorobenzene meets the criterion on bioaccumulation. BCF values for pentachlorobenzene range from 1085 – 23 000 L/kg for fish, 833 – 4 300 L/kg for mollusca, and 577 – 2258 L/kg for crustacean. Biomagnification may be expected due to the high $\log K_{ow}$ and the fact that biotransformation is insignificant. However, data on the biomagnification of pentachlorobenzene are lacking.

The available data support the potential for long range transport of pentachlorobenzene. The physical and chemical characteristics are within the range of the other POPs. Model estimations on the transport distance resulted in distances of 8 000 km, while estimates based on air measurements suggested 13 338 km. Monitoring data also indicate that PeCB is subject to long range transport. PeCB was detected in air and precipitation at various locations in the world, many of those

far from its sources. The small spatial variability across the Northern Hemisphere observed in some studies also indicate that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere.

A large quantity of monitoring data exists on PeCB detected in abiotic matrices as well as in biota in temperate zones, mainly originating from developed countries. In general, concentrations of PeCB in the temperate zones of the world seem to be decreasing. This pattern is representative for most POPs. For the Arctic and Antarctic area, only recent data are available which do not enable a trend to be derived.

Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified. The only risk phrase for pentachlorobenzene in the European ESIS database is R22, harmful if swallowed. Lowest LD50 observed for acute exposure was 250 mg/kg bw. Repeat-dose mammalian toxicity tests result in evidence of hepatic, nephric, hematological, and developmental toxicity for this chemical. According to the American Hazardous Substances Data Bank pentachlorobenzene is not classifiable as to human carcinogenicity because there are no human data and no animal data available. PeCB is moderately toxic to humans. Pentachlorobenzene is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. Data on soil and sediment organisms are limited or lacking.

Bioavailability of pentachlorobenzene is inversely proportional to the organic carbon content of the soil or sediment. However, experiments suggest that hydrophobic chemicals bound to the sediment or suspended sediment may act as a reservoir and result in continuous uptake. There are limited quantitative data on this process for pentachlorobenzene.

The data from Europe and North America show that production and use of pentachlorobenzene has ceased over the last decades, but it cannot be excluded that PeCB is produced or used elsewhere. Unintentional release of pentachlorobenzene as a byproduct of incomplete combustion appears to be the largest current source. However, this conclusion is based on data for Europe and North America only.

An important element in the assessment of the potential risk of PeCB is the assessment of the risk associated with intended and non-intended uses. This distinction is not possible with the current information but it should be very useful for the decision making process. Such an analysis would request precise information on the amounts released by intentional production and use in the past and the unintentional releases plus a correction for the degradation rate of the substance after release. Data on past production and use are currently lacking.

PeCB meets all screening criteria on long range transport, persistence, bioaccumulation and toxicity. Generally, environmental concentrations seem to be decreasing. Production and use have ceased in Europe and North America, but data from other parts of the world are limited. Unintentional release as a byproduct of incomplete combustion appears to be the most important source of PeCB in the environment.

The available information does not allow the Committee to distinguish between the environmental burden caused by intentional use and the burden caused by the unintentional production and releases of PentaCB. Clarifying this distinction would help the Committee to prepare the risk management evaluation and to formulate its final conclusions. Hence, additional data on this issue should be sought.

4   Concluding statement

PeCB is persistent in the environment and is bioaccumulative. The small spatial variability in the ranges of air concentrations across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere. There are monitoring data from remote areas, backed up by modelling results that suggest that pentachlorobenzene can be transported over great distances. Pentachlorobenzene is moderately toxic to humans, but is very toxic to aquatic organisms.

As a result of the long range transport of PeCB, neither a single country nor a group of countries alone can abate the pollution caused by this substance. Unintentional release of PeCB, as a byproduct of incomplete combustion, appears to be the largest current source. Measures to reduce these releases can only be taken at a global scale. Although the production and use of pentachlorobenzene seems to have ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment. Based on the available evidence, PeCB is likely, as a result of its long

range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

As the distinction between the environmental burden caused by intentional use and the burden caused by unintentional production and releases would support the preparation of the risk management evaluation and making the final recommendation, the Committee considers that an additional effort should be made to fill this gap.

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15 4% 2	FWMF FWMFs 1	0.5mg/kg/day IgG IgM	

**United Nations
Environment
Programme**

Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on alpha hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on alpha hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/17. The text of the risk profile, as amended, is provided below. It has not been formally edited.

K0820043   300108

ALPHA HEXACHLOROCYCLOHEXANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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Executive summary

Mexico, being a Party to the Stockholm Convention, proposed lindane as well as alpha- and beta-hexachlorocyclohexane to be included in Annex A, B or C of the Stockholm Convention. After the risk profile on lindane had already been agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that alpha-HCH also complied with the screening criteria laid down in Annex D of the Convention and that further elaboration of the proposal and preparation of a draft risk profile should be done.

After almost forty years of extensive use worldwide, there has been a gradual replacement of technical hexachlorocyclohexane (HCH) by lindane (gamma-HCH). No significant uses of technical HCH have been reported after 2000. However, releases into the environment may also occur from lindane production as well as from hazardous waste sites, landfills and contaminated sites. Because of its hazard profile and widespread abundance, technical HCH (including alpha-HCH as the main isomer) is subject to national and international regulations and prohibitions.

Alpha-HCH is susceptible to abiotic and biotic degradation at variable rates and degrees, depending on e.g. environmental media, site and climate. Alpha-HCH is expected to rapidly degrade in tropical conditions, whereas it accumulated in colder climates. Alpha-HCH is moderately persistent in soil. Based on values from aquatic compartments i.e. Arctic freshwater and sea water, it can be concluded that alpha-HCH shows high persistence in water in colder regions.

The physico-chemical properties of alpha-HCH allow the dispersal of the substance from its sources to the Arctic by a combination of long-range atmospheric transport and ocean currents. High levels of alpha-HCH have been detected in the Arctic Ocean, where it has built a large reservoir and is present in marine as well as in terrestrial species.

Alpha-HCH exposure levels in local areas have declined after worldwide prohibitions and restrictions. However regions with recent exposure and/or high pollution can still show elevated levels. A special concern also arises from exposure of hazardous waste sites and dumping grounds from disposed alpha-HCH residues from lindane production. Due to its persistence, alpha-HCH can still be detected regularly at low background levels in the environment. Elevated levels have also been reported from the Arctic (levels in the Arctic Ocean are higher than in temperate oceans and lakes). Though alpha-HCH levels in air decreased more than twenty-fold from the 1980s onwards, there has been only a modest change in higher marine and terrestrial predators e.g. fur seals or polar bears.

Because alpha-HCH is present in the terrestrial and aquatic food chains, alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The biomagnification factors (predator-prey comparison) for many of the examined species are greater than 1 (one). Some animals, especially birds, but also mammals, have the potential to metabolize alpha-HCH. As this is an enantioselective biotransformation, a distinctive accumulation of (+) or (-) alpha-HCH can occur in mammals (depending on the species).

Alpha-HCH is the isomer with the highest neurotoxic potential beside gamma-HCH. Alpha-HCH has been classified as possibly carcinogenic to humans (group 2B) by the International Agency for Research on Cancer (IARC), based on inadequate evidence of carcinogenicity in humans and sufficient evidence for carcinogenicity to animals. Alpha-HCH causes liver hyperplasia and liver tumours in (laboratory) rodents. From animal experiments it is known that alpha-HCH affects the immune system; immunosuppressive effects were observed in humans exposed to technical HCH as well. Epidemiological studies indicate an elevated incidence of breast cancer after exposure to alpha-HCH as well as hormonal disorders leading to infertility and abortions. A possible association with intrauterine growth retardation and aplastic anaemia has been postulated.

Based on the hazard profile and the exposure scenarios it can be concluded that alpha-HCH may adversely affect wildlife and human health in contaminated regions. The United States Environmental Protection Agency (USEPA) estimated, based on daily intake rates for the Arctic population, elevated cancer rates, though estimates are very conservative. It has to be considered that the liver is the target organ for all HCH-isomers, thereby leaving the risk of additive effects. Moreover the indigenous Arctic population as well as wildlife are exposed to a broad range of POPs including all HCH isomers and other pollutants leading to probably additive effects. Nevertheless Arctic public health authorities believe the significant social, cultural and economic benefits of traditional foods outweigh the risks of contaminants such as HCH at present but give another reason for the quick control and elimination of all HCH isomers from traditional foods.

For these reasons global action on alpha-HCH is warranted.

1   Introduction

In the proposal by Mexico to include lindane in Annex A, B or C of the Stockholm Convention and in the ensuing discussions, it was concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing alpha-hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/7). Austria (on behalf of Germany) prepared the first working draft on alpha-HCH.

Alpha-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Alpha-HCH is mainly stimulating to the central nervous system, but the final effect of the mixed isomers depends on the composition (IPCS, 2001). In general, HCHs are among the most studied pesticides with respect to their environmental fate and effects (Breivik et al., 1999).

1.1   Chemical Identity

Chemical name: Alpha-hexachlorocyclohexane (alpha-HCH)
IUPAC name: (1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane
Common synonyms: 1,2,3,4,5,6-hexachlorocyclohexane, alpha isomer, (1alpha,2alpha,3beta,4alpha,5beta,6beta)-1,2,3,4,5,6-hexachlorocyclohexane, alpha-1,2,3,4,5,6-Hexachlorocyclohexane; alpha-benzene hexachloride, alpha-BHC, alpha-HCH, alpha-lindane; benzene-trans-hexachloride, Hexachlorocyclohexane-Alpha (Chemfinder, 2007)

Alpha-HCH is a chiral molecule; the enantiomers are shown in Figure 1.
CAS number:
Racemic: 319-84-6, (+) alpha-HCH: 11991169-2, (-) alpha-HCH: 119911-70-5
Chemical formula: $C_6H_6Cl_6$
Molecular weight: 290.83

Figure1: Structure of alpha-HCH,
modified from Buser et al. (1995)
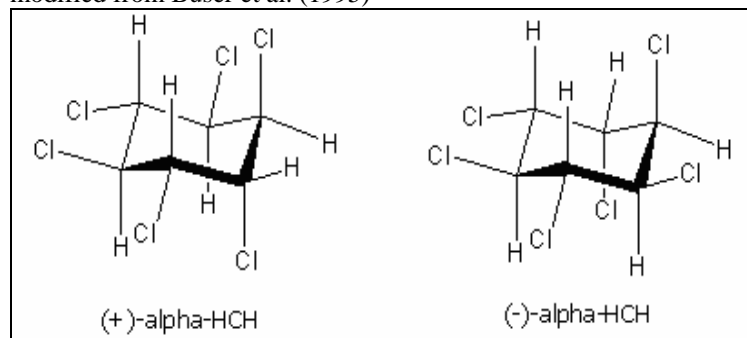
Stability and persistence of HCH isomers are attributed to the orientation of the chlorine atoms on the molecule. Axial chlorine atoms may probably provide available sites for enzymatic degradation. Alpha-HCH exhibits 4 axially and 2 equatorially orientated chlorine atoms. Thus it is thought that the molecule is more susceptible to degradation than the beta-isomer (Philips et al., 2005).

1.1.1   Physico-chemical properties

The physico-chemical properties (see Table 1 for selected properties) of alpha-HCH allow for long-range transport and "cold condensation", an enrichment of the substance in cold climates compared to concentrations near sources, on altitudinal and latitudinal scales described by Wania and Mackay (1996). Alpha-HCH can volatilize due to its vapour pressure and low octanol-air partition coefficient from soil surfaces. The Henry's law constant is relatively low and decreases with temperature.

Table 1. Selected physico-chemical properties

Melting Point (K)	432 [1]
Boiling Point (K)	561 [1]
Water solubility (mol*m^{-3} at 25 °C)	0.33 [2]
Vapour pressure (Pa at 25 °C)	0.25 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.74 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	7.5 [2]
Physical state	crystalline solid [1]

[1] ATSDR (2005)

[2] Xiao et al. (2004)

1.2   Conclusion of the POP Review Committee of Annex D information

The POP Review Committee evaluated the proposal regarding alpha-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/7 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/15) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/9 the Committee reached the conclusion that alpha-HCH meets the screening criteria specified in Annex D. The Committee also decided to establish an ad-hoc working group to review the proposal further and prepare a draft risk profile in accordance with Annex E of the Convention.

1.3   Data sources

The draft risk profile is based on the following data sources:

- Proposal submitted by Mexico for listing alpha-hexachlorocyclohexane in Annexes A, B and/or C of the Convention (UNEP/POPS/POPRC2./INF/7), 2006.

- Decision POPRC-2/9 of the Review Committee, 2006.

- Information submitted by Parties and observers according to Annex E of the Convention: specific and/or scientific information: Czech Republic, Germany, International POPs Elimination Network (IPEN), Japan, Switzerland, United States of America; general information: Algeria, Crop Life International, Kingdom of Bahrain, Mauritius, Mexico, Qatar, Republic of Lithuania and Turkey. This information is available on the Convention's website.
  (http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/submissions.htm).

- Assessment of lindane and other hexachlorocyclohexane isomers, USEPA, 2006.
  http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm

- International Programme on Chemical Safety, ALPHA- and BETA-HEXACHLOROCYCLOHEXANES, Environmental Health Criteria 123, World Health Organization. Geneva, 1992.
  http://www.inchem.org/documents/ehc/ehc/ehc123.htm

- Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2005.
  http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. 2006. North American Commission for Environmental Cooperation
  http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=2053

  In addition to these information sources, a literature search of public data bases was conducted. The following databases were used: ECOTOXicology database (Ecotox, http://www.epa.gov/ecotox/) Hazardous Substances Data Bank (HSDB, http://toxnet.nlm. nih.gov/cgi-bin/sis/htmlgen?HSDB), Pubmed (http://www.ncbi.nlm.nih.gov /entrez/query.fcgi?DB=pubmed), Environmental Fate Data Base (EFDB http://www.syrres. com/esc/efdb_info.htm. In general search terms include the chemical name or CAS number and/or a combination of technical terms because of the multiplicity of entries. For the same reason, specific topical and updated articles were also considered. The reports listed above contained individual references which have not been listed specifically in this draft risk profile. Additional references are provided in UNEP/POPS/POPRC.3/INF/27.

1.4   Status of the chemical under international conventions

Alpha-HCH is a constituent of technical HCH, which is regulated by at least two international agreements. The first one is the 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. Technical HCH is listed in Annex II of the protocol which restricted its use to an intermediate in chemical manufacturing only.

The second agreement is the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. HCH (mixed isomers) is subject to the PIC Procedure and is listed in Annex III of the Convention.

Canada, Mexico and the United States signed the North American Regional Action Plan (NARAP) on Lindane and other Hexachlorocyclohexane isomers in 2006. The goal of the NARAP is to reduce the risks associated with the exposure of humans and the environment.

In the European Union, the production and use of technical HCH as an intermediate in chemical manufacturing will be phased out by the end of 2007 at the latest (Regulation (EC) No 850/2004). HCHs are also among the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the alpha-isomer, are on the List of Chemicals for Priority Action under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. The objective is the prevention of pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances.

2   Summary information relevant for the risk profile

2.1   Sources

2.1.1   Production

Alpha-HCH by itself is neither intentionally produced nor placed on the market. It is produced as the main constituent of technical HCH which is used as organochlorine insecticide or chemical intermediate to manufacture enriched gamma-HCH (lindane). Currently no production data on technical HCH have been reported, whereas manufacture of lindane still takes place (IHPA, 2006).

HCH is manufactured by photochemical chlorination of benzene which leads to the formation of mainly five stable HCH isomers. The yields of different isomers vary due to technical differences in the production process. The reported ranges are: alpha-HCH (55 - 80%), beta-HCH (5 - 14%), gamma-HCH (8 - 15%), delta-HCH (6 - 10%) and epsilon-HCH (1 - 5%) (Breivik et al., 1999). Further details on the production and reuse of HCH residuals can be found in UNEP/POPS/POPRC.2/17/Add.4 (Risk Profile on Lindane) and IHPA (2006). The following countries which submitted information according to Annex E stated that there was currently no production or use of alpha-HCH: Czech Republic, Germany, Mauritius, Mexico, Norway, Qatar, Republic of Lithuania, Turkey, Switzerland, and the United States of America.

2.1.2   Trade and stockpiles

Technical HCH was rapidly introduced in the 1940s on a large scale on the market, due to its universal insecticidal properties. The promising market opportunities worldwide arose in the search for an inexpensive alternative to DDT (IHPA, 2006). However, due to the decreasing effectiveness of the gamma> alpha> beta-isomer in controlling insects (Baumann et al., 1980) technical HCH was gradually replaced by lindane (> 99% gamma-HCH). However, the manufacture of lindane has resulted in a huge amount of HCH residuals, which must be disposed of or otherwise managed. IHPA (2006) calculated 1.9 to 4.8 million tons of HCH residuals based on global lindane production, in the absence of exact data. These estimates are far beyond the values reported by Walker et al. (1999) who reported stockpiles of approximately 2 785 tons of technical HCH and 45 tons of unspecified HCH material in Africa and the Near East.

2.1.3   Uses

Around 10 million tons of technical HCH were released into the environment between 1948 and 1997 (Li et al., 1999). Breivik et al. (1999) estimated technical HCH usage at approximately 400 000 tons in Europe alone between 1970 and 1996. The data illustrate the large uncertainties of these estimates. According to Li and Macdonald (2005) global usage of technical HCH was dominated by 10 countries headed by China, which consumed almost half of the total global quantity. The other countries were (in order of decreasing usage): Former Soviet Union, India, France, Egypt, Japan, United States, East Germany, Spain and Mexico. Usage of technical HCH was banned in most western countries and Japan in the 1970s but continued in China and Russia until 1983 and 1990. In 1990, India also banned technical HCH for agricultural use but

kept it for public health uses (AMAP, 2004a). Technical HCH usage steadily declined and now technical HCH is virtually no longer used worldwide. However, there are indications that the use of stockpiles, limited use for public health purposes and/or illegal use cannot be excluded (Zhulidov et al., 2000; Bakore et al., 2004; Qian et al., 2006).

2.1.4 Releases to the environment

There are several pathways of alpha-HCH for entering the environment. Historically, alpha-HCH was released during the manufacture of technical HCH and its use as a pesticide. Alpha- and beta-HCH have the same global emission patterns which, however, differ in scale. Li and Macdonald (2005) estimated the global usage of alpha-HCH (based on data on technical HCH) at 6 millions tonnes, with 4.3millions tonnes emitted into the atmosphere. After the 1940s emissions of alpha-HCH increased and peaked in the early 1970s. Due to the ban on the use of alpha-HCH in North America, in European countries and Japan, emissions decreased but reached again a peak in the 1980s because of frequent usage in Asian countries. After the 1980s, figures dropped due to further prohibitions and restrictions e.g. in China. Releases of alpha-HCH into the environment are also possible from hazardous waste sites (USEPA, 2006), stockpiles and residues of lindane production, which are not always controlled or maintained safely (IHPA, 2006). Also, contaminated sites (e.g. from former production plants) may contribute to the environmental burden of alpha-HCH (Concha-Grana et al., 2006). Germany (submitted Annex E information, 2007) reported that there are still a few isolated local sources i.e. landfills and dumps in the former GDR (East Germany) from applications of technical HCH. As a result, higher concentrations of alpha-HCH in fish of the river Elbe near the former production site were detected after heavy rainfalls and floods in 2003. However, quantitative estimates of releases from hazardous waste sites and landfills are not available.

2.2 Environmental fate

2.2.1 Persistence

Alpha-HCH is, in principle, degradable in environmental compartments by abiotic processes such as photodegradation or hydrolysis. Based on laboratory experiments from Ngabe et al. (1993), hydrolytic half-lives of alpha-HCH show strong temperature dependence. At 20°C, pH 8 the DT50 was 0.8 years whereas it increased at lower temperature (5°C, pH 7.8) to 26 years. Based on these degradation rates Harner et al. (1999) calculated a DT50 of alpha-HCH in the Arctic Ocean of 63 years.

In general, HCH-isomers do not absorb light > 290 nm. Thus it is expected that photolysis plays a minor role in the removal of alpha-HCH. Deo et al. (1994) reported half-lives of alpha-HCH in aqueous solution exposed to sunlight of 4 to 6 days. While the mechanism of this degradation is uncertain, it was shown that alpha- as well as gamma-HCH break-down by indirect photolysis with photosensitizing agents that may transfer the excitation energy to HCH (ATSDR, 2005; USEPA, 2006). Regarding photodegradation on hard surfaces, a half-life equal to 91 hours on a thin film has been reported (ATSDR, 2005). However, the relevance of this result is questionable when taking into consideration the arguments mentioned above.
The measured atmospheric OH rate constant of 1.4×10^{-13} cm^3/molecule-sec resulted in a corresponding half-life of 115 days (ATSDR, 2005) (using an average hydroxyl radical concentration of 5×10^5 molecule/cm^3 according to the TGD (2003)).

In conclusion, abiotic degradation is very slow especially at lower temperatures. Photolysis in aqueous media and air is considered to play an insignificant role in the degradation of alpha-HCH.

Biotic degradation of alpha-HCH has been found to take place in pure cultures, soil slurries, soil (semi-)field studies, sediment and water. Initially it was thought that HCH biodegradation in soil occurs under anaerobic conditions. However, several investigations show that alpha-HCH is aerobically degraded, in some cases even faster than anaerobically. Breakdown was also reported for methanogenic and sulfate reducing conditions (Phillips et al., 2005).

The anaerobic metabolic pathway of alpha-HCH leads via dechlorination to tetrachlorocyclohexene. Dichlorophenol and trichlorophenol as well as chlorobenzene and benzene were formed under methanogenic conditions, the last two as stable end products. These metabolites can be further mineralised aerobically or anaerobically (Bachmann et al., 1988; Phillips et al., 2005). In pure cultures as well as in flooded soil gamma-HCH is the most easily dechlorinated isomer followed by alpha-HCH under anaerobic conditions (Jagnow et al., 1977; MacRae et al., 1967).

Under aerobic conditions alpha-HCH was dehydrochlorinated to pentachlorocyclohexane in soil slurries. Further conversion to tetrachlorobenzene or trichlorobenzene may occur to yield dichlorobenzene (Deo et al., 1994). The aerobic degradation pathway of gamma-HCH was extensively studied with *Shingobium sp.* and results in several metabolites. It was suggested that alpha-HCH follows the same pathway than gamma-HCH. Complete mineralization of alpha-HCH was shown in laboratory studies under aerobic conditions (Phillips et al., 2005).

In general, climatic conditions as well as soil texture and organic matter altering substance sorption, water content, pH and bacterial growth influence degradation rates (IPCS, 1992). The moisture content of the soil enhances losses of alpha-HCH, which is attributed to higher volatility and/or microbial degradation (Chessells et al., 1988; Phillips et al., 2005). Bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported (Phillips et al., 2005).

Data on laboratory soil studies or field investigations are limited. Under various field conditions it is assumed that degradation rates are in the order of alpha > gamma > > beta (Suzuki et al., 1975, Stewart and Chisholm, 1971; cf. also section 1.1). Singh et al. (1991) reported field half-lives (i.e. dissipation, including losses by leaching and volatilisation) of around 55 days on cropped and uncropped plots in a sandy loam in India under subtropical conditions. This result is consistent with findings from Kaushik (1989) who reported an even shorter half-life for technical HCH under similar study conditions. Also, in temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil > 50 % removal after 161 days, mainly attributed to a quick decline in the first few weeks, whereas degradation slowed down afterwards. Suzuki et al. (1975) also suggested that low residue levels (below 0.1 ppm) may resist microbial and physico-chemical action. Low concentrations of alpha-HCH may persist in the environment indefinitely because of low affinity of enzymes or transport system responsible of HCH degradation (Phillips et al., 2005). Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 4 % of the alpha-isomer after 15 years in a sandy loam in Canada. In addition, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, alpha-HCH with the highest initial concentration is substantially less prevalent in the field and the detected levels were twice as much as the levels of the gamma-isomer.

Abiotic processes are not enantioselective, but biodegradation may be. If nonracemic alpha-HCH residues in the environment or biota are measured, enzymes are involved. However, racemic residues do not exclude the possibility of biotic degradation (cp. Suar et al., 2005). Also for monitoring purposes enantiomeric fractions (EFs, calculated by the formula EF = ER/(ER+1), ER = enantiomeric ratio: (+) /(-) alpha-HCH, Kallenborn et al., 2001) have been quantified for the characterisation of residues. Hegeman and Laane (2002) investigated the enantiomeric distribution of alpha-HCH in different environmental compartments obtained from 618 measurements. In general, the abiotic compartments showed average EFs close to 0.5. In soil, the preference tended to be the degradation of the (-) alpha-HCH (EF > 0.5), whereas in water an opposite tendency was found. Kurt-Karakus et al. (2005) reported a range of EFs for alpha-HCH of 0.4 - 0.89 (mean 0.5) in global background soils which covered a greater range than the EFs in ambient air of North America (0.47 - 0.52), suggesting that post-deposition degradation had taken place. However, since EFs vary considerably with site, caution is needed when using enantiomeric signatures in the air as a marker of reemissions from (soil) surfaces.

Based on the K_{oc} value and confirmed by field data, alpha-HCH is expected to have a low leaching potential (HSDB, 2006; Singh et al., 1991). However, groundwater pollution may occur in highly contaminated areas (Law et al., 2004). Detailed information regarding the relevance of isomerisation in the environment can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4).

Alpha-HCH is able to biodegrade in sea water/sediment samples (HSDB, 2006) and freshwater (Padma and Dickhut, 2002). Helm et al. (2002) estimated the half-lives for alpha-HCH in a high Arctic lake at 0.6 to 1.4 years. For the Eastern Arctic Ocean enantioselective degradation for the (+) alpha- and (-) alpha-HCH with half-lives of 5.9 and 23.1 years was observed. If breakdown with hydrolysis was taken into consideration, the overall half-lives were 5.4 and 16.9 years for the (+) and (-) alpha-isomer respectively (Harner et al., 1999). Though sediment degradation rates are poorly known and thus the estimates are less certain, the half-life for alpha-HCH in sediments of a high Arctic lake was assumed to be approximately 2 years (Helm et al., 2002). Some data on α-HCH levels in sediment cores 30-40 years of age indicate long half-lives of α-HCH in sediments from different geographical areas (Barra et al., 2001; Rawn et al., 2001; Riching et al., 2005)

2.2.2   *Bioaccumulation*

The octanol-water partition coefficient (log Kow = 3.8) for alpha-HCH indicates a potential for bioaccumulation (ATSDR, 2005), though it is below the value of 5 stated in Annex D paragraph 1(c)(i) of the Stockholm Convention. A wide range of bioconcentration factors (BCFs) have been reported in several studies. For green algae, bioconcentration factors varied from about 200 in *Chlorella pyrenoidosacells* to 2700 (dry weight basis) and 13000 on a lipid basis, respectively in *Dunaliella*. Studies of invertebrates show BCFs in the range of 60 (8000 on a lipid basis) in *Artemia* to 2700 in polychaetes, depending on the lipid content of the animals (IPCS, 1992).

The BCF (whole body) for alpha-HCH according to the former OECD test guideline 305 E in zebra fish was equal to 1 100 under steady state conditions with uptake constants (k1) of 50 and clearance rate constants (k2) of 0.045. These values are similar to those of gamma-HCH (BCF 850, k1 = 50.8, k2 = 0.055) (Butte et al., 1991). Oliver et al. (1985) reported BCFs (whole body) ranging from 1 100 to 2 800 in rainbow trout.

In general, studies from Arctic marine food webs show food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, greater than 1. The BMFs (biomagnification factor, predator-prey comparison) of alpha-HCH in zooplankton and Arctic cod are greater than 1, showing a potential for biomagnification. BMFs of alpha-HCH in seabirds were generally less than 1 with the exception of dovekie and black guillemot. Ringed seals showed a BMF of 2.5 (Moisey et al., 2001). It is suggested that alpha-HCH isomer has the potential to biomagnify in aquatic food webs and may increase at lower as well as in upper trophic levels, especially in marine mammals (USEPA, 2006; Hoekstra et. al., 2003a). The report of Hoekstra et al. (2003b) also confirms this presumption with a BMF of 9.85 in bowheads for alpha-HCH.

Fisk at al. (2001) reported on the influence of chemical and biological factors on the trophic transfer of POPs including alpha-HCH. In general, the highest BMF should be seen in homeothermes (birds and mammals) compared to poikilothermes (fish, invertebrates) attributed to their greater energy requirements. Within the homeothermes, seabirds usually have the highest BMFs, consistent with the greater energy demand in birds. But this is not applicable for alpha-HCH. Most seabirds appear to be able to induce the cytochrome P450 such as CYP2B, which are enzymes to metabolize alpha-HCH, so the ranking from highest to lowest biotransformation ability (usually for OCs: marine mammals > seabirds > fish > zooplankton) is not applicable for this compound. The BMF of alpha-HCH in poikilothermes is 1.3 and equal to that in homeothermes (Hop et al., 2002).

As alpha-HCH is a chiral compound, the determination of the ER or EF is important in order to understand species-specific metabolism and biotransformation. No enantioselective biotransformation in rainbow trout for alpha-HCH was observed by Konwick et al. (2006) in a dietary study showing consistent EFs in the fish. In an experiment of Wong et al. (2002) alpha-HCH was racemic throughout the course of the experiment with rainbow trout, fed with treated food. These results are in contrast with reports of enantioselective biotransformation in other species. The EF in benthic invertebrates, zooplankton and fish was 0.45 as a maximum. Ringed seals showed an EF of 0.51, while the EFs in seabirds range from 0.65 (dovekie) to 0.97 in glaucous gulls (Moisey et al., 2001). This suggests that seabirds preferentially metabolize the (-) enantiomer. Associated with a BMF of < 1 in seabirds, it has been found that both enantiomers of alpha-HCH are metabolized in birds (dovekie and black guillemot seem to have a lower capacity).

The EF of 0.51, considered together with the BMF of 2.5 in seals, indicates that mammals are not able to biotransform alpha-HCH in great amounts (Moisey et al., 2001). Nevertheless, Wiberg et al. (2000) found residues of alpha-HCH with nonracemic ERs in seals as well as in polar bears. According to Hoekstra et al. (2003b) accumulation of the (+) enantiomer occurs in bowhead whale and beluga, but (-) alpha-HCH enriches in bearded seal. Ringed seal show a slight accumulation of the (+) enantiomer (Hoekstra et al., 2003b) but sometimes the alpha-HCH residues are racemic (Fisk et al., 2002). This indicates an enantiospecific biotransformation and accumulation of alpha-HCH in the food chain. When investigating the EFs in krill, cod and penguin eggs, Corsolini et al. (2006) also found enantioselective biotransformation with an increase by 14 % of (+) alpha-HCH from the lower to the higher trophic level (from krill to penguin). There are interspecies differences in the enantiomeric profile of alpha-HCH in marine mammals, too. The BMF for calanus to bowhead for example is high (near 10 with a (+) alpha-HCH fraction of 16 and 4.5 of (-) alpha-HCH) (Hoekstra et al., 2003b).

Moisey et al. (2001) showed different BMFs in doveky, depending on the prey. Summed up, biomagnification is affected by many parameters such as contamination in biota, and consequently of food (prey), the trophic level and the ability to biotransform alpha-HCH.

Kelly at al. (2007) have recently shown that, for substances with a log Koa >6 and a log Kow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is also well illustrated by beta-HCH, in the marine mammalian and terrestrial food webs. as such compounds biomagnify strongly up to 3000- and 400-fold respectively. Alpha-HCH also meets these criteria.

Not only in the arctic food web, but also in organs of fur seals from the Pacific coast of Japan and double crested cormorants from the great lakes, alpha-HCH was detected (with an alpha-HCH ER from 1 in the muscle to 1.58 in fat). High alpha-HCH ERs were found in the brain of the cormorants (> 3.6) (Iwata et al., 1998). Willet et al. (1998) inferred from high alpha-HCH concentrations in marine mammal brain that this compound can cross the blood/brain barrier. Ulrich et al. (2001) also found in studies with rats that the alpha-HCH ER in brain, ranging from 2.8 to 13.5, is not caused by an enantioselective metabolism but that selective retention might be responsible.
Braune et al. (1999) detected alpha-HCH residues in the fat of caribou. Residues of alpha-HCH could also be found in livers and the adipose tissue of arctic foxes. The alpha-HCH ER of 2.2 in the liver, and 1.1 in the adipose tissue, indicates a stereoselective bioaccumulation also in terrestrial mammals (Klobes et al., 1997).

In conclusion high levels are found in Arctic biota because of the bioaccumulation potential of alpha-HCH (as a product of bioconcentration and biomagnification) and the historically particularly efficient deposition processes of this substance in the Arctic waters. The efficient accumulation is an effect of the combination of the physico-chemical properties of

alpha-HCH and the low temperature in the Arctic. In other words, alpha-HCH effectively accumulates in the Arctic ecosystem as a whole.

2.2.3   Long range environmental transport

Monitoring data on the environment including biota from remote regions such as the Arctic or Antarctica, where technical HCH has not been used, provide evidence of the long-range transport potential of alpha-HCH. Also the physico-chemical properties in combination with its stability allow alpha-HCH to undergo long range transport in the atmosphere. Primary emissions from the source regions (mainly in Asia) and Arctic air concentrations have synchronously decreased, suggesting a rapid dispersion of alpha-HCH from its sources to remote regions (Li and Bidleman, 2003). Especially high concentrations compared to the source regions were reported for the Arctic Ocean (see Table 2). It is assumed that after long range transport alpha-HCH accumulated in the cold water due to its low Henry's law constant and built a large reservoir (Li and Macdonald, 2005). HCHs including alpha-HCH are the most abundant pesticides in the Arctic air and water (Walker et al., 1999).

To understand pathways and the fate of alpha-HCH in the upper Arctic Ocean, Li et al. (2004) developed an Arctic Mass Balance Box Model. They concluded that the highest load of 6 670 tonnes was reached in 1982 mainly by gas exchange and ocean currents and decreased thenceforward by an average annual rate of approximately 270 tons/year. After 1990, ocean currents become the dominant input of alpha-HCH in the Arctic Ocean. However, the portion of alpha-HCH entering the Arctic atmosphere via long range transport from source regions played a prominent role (especially in the beginning). After the early 1990s alpha-HCH in the Arctic air came from both atmospheric transport and volatilization from the Arctic Ocean. It was suggested that a complete elimination of alpha-HCH mainly by degradation and ocean currents would require another two decades. In total 27 700 tons alpha-HCH were transported between 1945 and 2000 via long range transport to the Arctic Ocean.

According to model calculations with the OECD Pov and LRTP Screening Tool, alpha-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and organochlorine pesticides (Wegmann et al., 2007). Model input properties of the chemicals include partition coefficients in air-water and octanol-water as well as half-lives in air, water and soil and the Henry's Law constant (based on figures contained in UNEP/POPS/POPRC2./INF/7). The model considers all environmental compartments quantitatively. The results of the model do not indicate absolute levels in the environment but help to compare possible POPs with identified POPs (reference chemicals: PCB congeners 28, 101, 180, HCB, carbon tetrachloride and alpha-HCH) according to their environmental persistence and potential for long range transport. Uncertainties in the chemical properties were investigated by Monte Carlo uncertainty analysis.

2.3   Exposure

Exposure to alpha-HCH resulted from the use of technical HCH, and from the production and manufacture of technical HCH and lindane. Because of the persistence high exposure is also expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles. Though usage of technical HCH has practically ceased worldwide monitoring data based on the ratio of the alpha-/gamma-isomer still suggest possible releases of technical HCH in certain areas (Zhang et al. 2003; Qian et al., 2006; Zhulidov et al., 2000).

Human exposure to alpha-HCH results mostly from ingestion of contaminated plants, animals and animal products. Inhalation of ambient air and consumption of drinking water are further sources of exposure, although to a minor extent. As shown by a French pilot study alpha-HCH was detected in indoor air and on the hands of the general population in the Paris area in 42 and 35 % of the samples. Levels were low and ranged up to 1.8 ng/m^3 in air and up to 8.5 ng/hand (Bouvier et al., 2006).

Monitoring data from a wide range of biota including humans suggest that significant uptake from the environment occurs, which demonstrates the bioavailability of alpha-HCH. Infants may be exposed during fetal development and breastfeeding.

2.3.1   Environmental monitoring data from local areas

Generally, environmental levels in local areas have dropped after restrictions and prohibitions of the usage of technical HCH (IPCS, 1992; see also Table 2). However, monitoring data show its ubiquitous distribution in all environmental media e.g. in monitoring activities in the Czech Republic (submitted Annex E information by the Czech Republic, 2007), in lichens of various locations in Switzerland (values given in table 2) or in a recently performed monitoring programme in Japan. Alpha-HCH had been detected in Japan in all but 7 fish specimens. The reported values are as follows: water 0.013 - 5.7 ng/l, sediment trace - 5.7 ng/g dw (dry weight), shellfish up to 1.8 ng/g ww (wet weight), fish up to 2.9 ng/g ww, bird 0.1 - 1.6 ng/g ww, air (warm and cold season) 0.02 - 3.2 ng/m^3 and 0.01 - 0.68 ng/m^3 (submitted Annex E information by Japan, 2007).

Table 2. Selected monitoring data of abiotic compartments and vegetation (values refer to alpha-HCH except otherwise stated)

Compartment	Country/region	Levels	Comments	References	Year
Air	Great Lakes, rural	< 1 - 84 pg/m^3	alpha-HCH, mean values, gas phase	Sun et al., 2006b	1992-2003
	Great Lakes, Chicago	52 pg/m^3	alpha-HCH, mean value, gas phase	Sun et al., 2006b	1996-2003
	Niigata, Japan	92 pg/m^3	Annual average, according to the authors a result of long-range trasport	Murayama et al., 2003	2000-2001
	Czech Republic (Kosetice)	**38**/21/17/22/**13** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1999-2003
	Finland (Pallas)	**24**/28/18/15/17/18/**9** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1996-2003
	Iceland (Storhofdi)	**17**/16/15/15/10/8/10/5/**7** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2003
	Norway (Lista)	**94**/94/76/69/52/61/50/37/25/19/17/17/**12** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1991-2003
	Sweden (Aspvreten)	**43**/57/61/50/-/67/**16** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2002
	Ny-Aslund (Svalbard, Norway)	73 pg/m^3	∑HCHs, mostly alpha-HCH, highest annual average value reported in 1996	AMAP, 2004a	1996-1988
	Barents Sea and eastern Arctic Ocean	11 - 68 pg/m^3		Harner et al. (1999)	1999
	Arctic	23 +/- 10 pg/m^3	Uniform distribution, arithmetic mean, measurements from 4 Arctic sites	Su et al., 2006	2000-2003
Precipitation	Belgium (Knokke)	4.1 - 0.5 ng/l	annual mean concentrations	EMEP measurement data online	1996-2003
	Germany (Zingst)	1 - 0.3 ng/l	annual mean concentrations	EMEP measurement data online	1999-2003
	Finland (Pallas)	< 1 ng/l	precipitation + dry deposition annual mean concentrations	EMEP measurement data online	1996-2003
	Norway (Lista)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1991-2003
	Sweden (Aspvreten)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1995-2002
	Canada/Great Lakes	1 - 40 ng/L	81 samples	IPCS, 1992	1976-77
Soil	Russian Arctic	0.2 - 0.5 ng/g dw	∑HCHs, predominantly alpha-HCH, soil including peat and litter	AMAP, 2004a	200-2001
	Antarctica	< 0.01 – 0.026 ng/g dw		Borghini et al., 2005	1999
Seawater	Northern Barents Sea, Eastern Arctic Ocean	910 (350 - 1630) pg/l	Sample period: July-September	Harner et al., 1999	1996
	North American Arctic Ocean	~ 7.5 µg/m^3		Li and Macdonald, 2005	1983
	Canadian Archipelago and southern Beaufort Sea	3.5 (1.1 – 5.4) ng/L	Surface water, measurements in summer	Bidleman et al., 2007	1999
Freshwater, rivers	Russian north rivers	< 1 - 69 ng/l	Seven-year weighted mean concentrations	AMAP, 2004a	1190-1996
River and estuarine waters	Eastern and southern Asia and Oceania	up to max. 470 ng/l		Iwata et al., 1994	1989-1991
Sediment (Lake)	Southern Sweden	9.2 ± 6.3 ng/g dw	∑HCHs, data from the Swedish Monitoring Program, 2002	AMAP, 2004a	2002
Vegetation (lichen)	Taymir (Russia)	7 ng/g dw	Highest concentration in lichen compared to samples from Alaska, Urals and Kola	AMAP, 2004a	1991-1993

Compartment	Country/region	Levels	Comments	References	Year
	Switzerland	0.5 - 4 µg/kg dw	From various locations (e.g. cities, industry, rural)	Submitted Annex E information by Switzerland, 2007	2002
Moss	Antarctica	0.43 – 4 ng/g dw		Borghini et al., 2005	1999

Environmental levels can still be high in the proximity of sources. HCH concentrations in contaminated soil of 40 - 225mg/kg were found in the topsoil around a chemical plant in Albania (UNEP, 2003). Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, Russian soils near the Lena River contained 0.001 - 0.017 mg/kg HCH (UNEP, 2003). Levels of up to 12 000 mg/kg were detected in soil of a highly polluted area in Spain (Concha-Grana et al., 2006)

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998). E. g. concentrations of HCHs (mainly the alpha-isomer) in several fish species from India ranged between 6 to 68 ng/g ww. Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of alpha-HCH of 0.5 ng/g ww (UNEP, 2003).

Alpha-HCH was also determined in eggs of Dalmatian Pelican (*Pelecanus crispus*) as well as in eels (*Anguila anguila*), the main pelican prey species collected in the wetlands of Amvrakikos Gulf in Greece for a two year period, 1992 and 1993. The concentration in pelican eggs was 7.9 ± 3.2 ng/g and 6.5 ± 2.5 ng/g ww in eels (UNEP, 2003). Concentrations of alpha-HCH in perch from the Latvian coast were up to 21 ng/g lw (lipid weight) (range 50 - 60), which were considered as background load. Elevated levels of up to 126 ng/g lw were attributed to a recent discharge of technical HCH (Olsson et al., 1999).

A local source of alpha-HCH was the usage of technical HCH by indigenous human populations in the Russian north against nuisance insects parasitizing domesticated reindeer (Li et al., 2004). However, no quantitative estimates of these exposure levels exist.

2.3.2   Exposure as a result of long range environmental transport

Highest measured levels of alpha-HCH have been reported for higher latitudes in air (e.g. Svalbard, Alert) as well as in seawater (Harner et al., 1999). As shown in table 2, alpha-HCH in air (e.g. from 94 pg/m^3 in 1992 to 12 pg/m^3 in 2003 in Norway) has decreased. AMAP (2004a) also summarized that concentrations of HCHs in Arctic air have been low since the mid 1990s due to worldwide prohibitions and restrictions. Before, in the 1980s, levels as high as approximately 900 pg/m^3 were measured in Arctic air (Li et al., 2002). Seawater levels in the eastern Arctic Ocean were generally lower than in the western part (Harner et al., 1999). Surface concentrations are highest in the Central Canadian Arctic Archipelago, intermediate in the Beaufort/Chukchi Seas and at the North Pole. In the 1990s levels in the Canadian Arctic Ocean were higher than anywhere else in the global marine environment (AMAP, 2004a).

This spatial distribution is also reflected in the levels in biota. Hoekstra et al. (2002) found that bowhead whales exhibit a reversal in their blubber alpha-/beta-HCH ratios on their migration route between the Bering to the Beaufort Sea. Levels in beluga blubber decreased from approximately 190 to 140 ng/g lw between 1982 and 1997 in the southeast Baffin Bay (AMAP, 2004a). Levels of up to 196 ng /g ww were reported from Alaska (submitted Annex E information by IPEN, 2007) and of up to 344 ng/g ww from Arviat (Stern et al., 2005). Minke whales from Greenland had higher concentrations of the prevalent alpha-isomer in blubber (mean levels 40 - 55 ng/g ww), than individuals from the North Sea (below 30 ng/g) (AMAP, 2004a). No decline of ∑HCHs in blubber of narwhal from the Canadian Arctic was observed between 1982 and 1999.

Concentrations in ringed seal of the Canadian Arctic showed no significant change of ∑HCH concentration from the 1970s. The elevated residues of HCH isomers in marine mammals of the Canadian Archipelago are likely due to the high concentrations of HCH isomers in the water because HCH isomers are the most abundant organochlorines in the Arctic Ocean (NARAP, 2006).

No temporal trend for Arctic cod and dab from the costal waters of Iceland was found for the period from 1991 to 2000, whereas results from Norway revealed a significant decrease (from 23 to 4 ng/g lw) of alpha-HCH residues in Arctic cod liver between 1987 to 1998 (Sinkkonen and Paasivirta, 2000).

Alpha-HCH has been detected in the muscle and liver of Arctic foxes (1.5 and 3 ng/g ww) in Canada (AMAP, 2004a). Levels in polar bear also reflect the spatial distribution of alpha-HCH being highest in Alaskan populations (in male polar bear up to 593 ng/g lw). No decline of alpha-HCH levels were reported for female polar bears in western Hudson Bay (concentrations up to 260 ng/g lw) from 1991 – 2002 (Verreault et al., 2005). Residues of alpha-HCH in East Greenland polar bears increased from 18 - 25 % during the 1990s (AMAP, 2004a).

2.3.3 Food

Daily intake values of alpha-HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be 0.008 µg/kg. In the USA, the age dependent average daily intake of alpha-HCH declined from 3.3 – 16.1 ng/kg bodyweight (bw; 1982 – 84) to 0.5 – 2.7 ng/kg bw (1986 – 91) (ATSDR, 2005). In the Total Diet Study conducted by FDA in 2003 on 100 food items, alpha-HCH was detected in 35 items (submitted Annex E information by IPEN, 2007). In a Total Diet Study from Canada (1993 - 96), an average daily dietary intake of 0.37 ng/kg bw alpha-HCH was reported (Health Canada, 2003, in EFSA, 2006). Within the European countries, representative dietary intake studies are scarce. One was performed in the Czech Republic. The median daily intake values for alpha-HCH declined from 4.3 ng/kg bw in 1994 to 1.6 ng/kg bw in 2002 (EFSA, 2005). A local diet study carried out in Spain in the years 1990/91 estimated daily intakes below 0.1 µg alpha-HCH (Urieta et al., 1996).

Alpha-HCH has been found in cow's milk in countries where HCH had been used recently. Mean levels of alpha HCH in cow's milk of two different regions in India were 0.012 mg/kg lipid and 0.0045 mg/kg lipid, respectively (ATSDR, 2005). 140 bovine milk samples from 14 districts of Haryana, India (sampled within 1998 - 1999) were analysed for organochlorine pesticide residues. Four percent of the samples exceeded the maximum residue limit (MRL) of 0.05 mg/kg as recommended by WHO for alpha-HCH (Sharma et al., 2006). A monitoring study (192 samples) of cow's milk from Mexico revealed 0.001 - 0.201 mg/kg alpha-HCH (ATSDR, 2005).

Fish and clam samples from India contained 0.01 – 0.02 mg/kg ww and 0.26 mg/kg ww alpha-HCH respectively (Nair and Pillai, 1992). High levels of alpha-HCH in the food chain are documented for the arctic region (AMAP, 2004b; levels are reported under section 2.3.2.). Indigenous populations in the Arctic are particularly vulnerable from dietary exposure to alpha-HCH through subsidence food such as caribou, fish, seal and whale.

2.3.4 Body burden

Median levels of alpha-HCH in 25 American patients were 0.04 ng/g in the whole blood and 1.1 ng/g (maximum 9.6 ng/g) in biopsy fat (ATSDR, 2005). A Spanish study reported mean alpha-HCH levels of 1.43 µg/g (maximum 6.75 µg/g) in fat samples of children living in farm areas (Olea et al., 1999). Alpha-HCH has been detected in 1.7 % of the 4822 blood samples of German adults from 120 locations (detection limit: 0.1 µg/l) (Becker et al., 1998). Alpha-HCH was detected in blood serum from three of 186 (=1.6 %) Brazilian children (mean: 1.8 ppb) (ATSDR, 2005). Alpha-HCH has been detected in all samples (n = 142) of an eastern Romanian study in 2005 with a median concentration of 31 ng/g lipid (range 3 - 146 ng/g) (Dirtu et al., 2006). High concentrations were reported for India, due to agricultural use and malaria control. Blood serum contained up to 0.45 mg/l alpha-HCH, whereas adipose tissue contained up to 0.30 mg/kg. Breast milk contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Scheele et al. (1998) investigated levels of several organochlorine compounds including alpha-HCH in bone marrow of 29 adults from Germany (collected between 1980 and 1991). Compared to adipose tissue, with generally highest levels of organochlorine compounds, alpha-HCH concentrations were 10-fold higher in bone marrow (mean: 0.050 mg/kg on dry lipid weight; max: 0.476 mg/kg). Alpha-HCH has also been detected in semen (ATSDR, 2005).

2.3.5 Exposure of children

Children are at specific developmental stages more vulnerable to risks from chemical substances than adults. It is unclear if children are more susceptible than adults to health effects from exposure to alpha-HCH although it is known that the developing brain is sensitive to the effects of different POPs. The specific enrichment of alpha-HCH in the mammalian brain might be a reason of concern. Placental transfer of alpha-HCH in humans is well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Alpha-HCH accumulates to a higher extent in human placenta than in breast milk.

Mean alpha-HCH levels in breast milk of a Finnish cohort (43 mothers, 1997 – 2001) were 0.19 ng/g lipid, whereas placenta mean concentrations of alpha-HCH were 3.47 ng/g lipid. In a Danish cohort (43 mothers, 1997 – 2001), mean concentrations of 0.51 ng/g lipid in breast milk and 1.53 ng/g lipid in placenta were detected. A specific metabolic activity of the placental tissue is suspected (Shen et al., 2006). It could be shown that in case of restrictions of use, alpha-HCH concentrations in breast milk decline continuously. In Germany alpha-HCH was still found in 28 % of the breast milk samples analysed in 1984/85 whereas it could not be detected in 1990/91 and 1995 samples (Ott et al., 1999). More than 2 000 individual human milk samples from women living in Western Germany collected and analysed between 1984 and 2001 indicated that alpha HCH concentration declined from > 0.01 mg/kg fat to levels below detectability (detection limit of 0.001 mg/kg fat) (Fürst, 2004). In the framework of the 3rd WHO human milk field study, HCHs were analysed in 16 human milk pools from ten European countries. In Bulgaria, Russia and Ukraine, alpha-HCH was detected in

concentrations between 0.002 – 0.006 mg/kg lipid, whereas in the samples of Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway and Spain alpha-HCH was not detectable (detection limit: 0.001 mg/kg lipid). In Nairobi, Kenya, 8.8% of 216 breast milk samples contained detectable alpha-HCH with a mean concentration of 0.013 mg/kg milk fat and a range of 0.002 – 0.038 mg/kg (Kinyamu et al., 1998). Breast milk samples from India contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Another Indian study reports 0.045 mg/l alpha-HCH in breast milk (Nair et al., 1996). It can be concluded that alpha-HCH concentrations in breast milk strongly depend on exposure and that in several East European and developing countries concentrations are still very high.

2.4   Hazard assessment for endpoints of concern

Compared to technical HCH and lindane, limited data are available for alpha-HCH. A limited number of subchronic and chronic oral toxicity studies exist. No animal studies of the toxicity of alpha-HCH via inhalation and dermal application have been conducted. Studies on developmental, teratogenic and reproductive effects of alpha-HCH are missing. There is a lack of dose-response data after oral exposure for all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For more details please consider the reports listed under heading 1.2.

Acute Toxicity/ Neurotoxicity: Oral LD50 values range between 1000 and 4000 mg/kg bw for mice and between 500 and 4 674 mg/kg bw for rats. The signs of poisoning were central nervous stimulation: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions, and cramps (IPCS, 1992).

Subchronic toxicity: In a 90-day study on rats carried out with dose levels of 0, 2, 10, 50, or 250 mg alpha-HCH/kg diet, growth was retarded and relative weight of organs (liver, heart, kidneys, and adrenals) increased at 250 mg/kg diet (equivalent to 12.5 mg/kg bw/day). At levels of 50 and 250 mg/kg, liver enzyme activities were modified and liver parenchyma cells enlarged. Liver weight increased at dose levels of 10 mg/kg diet (equivalent to 0.5 mg/kg bw/day) and reductions in white blood cell count were noted. Signs of immunosuppression (reduced serum levels of immunoglobulins G and M) were observed at 50 and 250 mg/kg diet. The NOAEL was 2 mg/kg alpha-HCH/kg diet (equivalent to 0.1 mg/kg bw/day; the LOAEL was 10 mg/kg diet) (IPCS, 1992).

Chronic Toxicity: When groups of 10 female and 10 male weanling Wistar rats were administered daily diets containing 0, 10, 50, 100, or 800 mg alpha-HCH /kg food (in corn oil) for 107 weeks, the highest dose level resulted in growth retardation, increased mortality, and slight kidney damage. With daily doses of 100 or 800 mg/kg, liver enlargement and histopathological changes in the liver were found. However, there were no liver changes at 50 mg/kg diet (NOAEL 50 mg/kg, LOAEL 100 mg/kg diet) (Fitzhugh et al., 1950).

Genotoxicity: Alpha-HCH was not mutagenic to bacteria (*Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537) with and without metabolic activation and did not induce DNA damage in bacteria. However, alpha-HCH induced DNA-fragmentation in human and rat hepatocytes. Oral exposure to alpha-HCH resulted in mitotic disturbances including an increased mitotic rate and increased frequency of polyploid hepatic cells in mice (ATSDR, 2005).

Carcinogenicity: Studies of the carcinogenicity of alpha-HCH are limited. Several studies in mice were performed, but their value is limited. Nevertheless, it is clear from the results that alpha-HCH, at high dose levels, produces nodular hyperplasia and hepatocellular carcinomas in mice (the incidence varying according on the strain) and also in rats (low incidence). Studies on initiation promotion and mode of action indicate that the neoplastic response observed with alpha-HCH is most likely due to a non-genotoxic mechanism. Alpha-HCH has been shown to promote tumors in the liver of mice and rats (IPCS, 1992). The International Agency for Research on Cancer (IARC) classified alpha- HCH in group 2B: possibly carcinogenic to humans. USEPA categorized alpha-HCH as probable human carcinogen. The department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Immunotoxicity: Mice, treated with alpha-HCH (50 and 250 mg/kg/day- i.e. 0.5 and 2.5 mg/kg/bw/day) showed signs of immunosuppression (reduced serum levels of immunoglobulins G and M).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported for workers exposed to technical HCH during pesticide or fertilizer formulation. Workers suffered from paraesthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme and IgM levels were enhanced (ATSDR, 2005). Inhalation of HCH (mixed isomers) may lead to irritation of the nose and throat (IPCS, 2006). The observation of serious hepatic effects in animals (e.g., fatty degeneration and necrosis) suggests that the same results could potentially occur in workers following prolonged occupational exposure to HCH isomers.

A German study on organochlorine compounds in the peripheral blood of 486 women with hormonal disorders and/or infertility revealed that alpha-HCH concentrations were significantly higher in women with uterine fibroids, antithyroidal antibodies, luteal insuffiency and women highly susceptible to allergies. Obese women and women with a history of abortion had the highest HCH levels in blood (Gerhard, 1993).

In a pilot study with limited statistical power a possible association between exposure to organochlorines and the risk of childhood aplastic anaemia was shown. Alpha-HCH was significantly higher in children with aplastic anaemia than in those of controls ($p < 0.05$) (Ahamed et al., 2006).

The association between alpha-HCH exposure and intrauterine growth retardation (IUGR, < 10th percentile of birth weight for gestational age) was examined in India. Statistically significant associations ($p < 0.05$) between maternal blood levels of alpha-HCH and interauterine growth retardation were found (Siddiqui et al., 2003)

Effects in non-target organisms: Data on effects in non-target species are extremely limited. Alpha-HCH is acutely toxic to aquatic organisms. Effect concentrations in algae, zooplankton (brine shrimp and water flea) and fish of < 1 mg/l were reported (detailed values in IPCS, 1992; ECOTOX database, 2007). A LC50 of approximately 1.4 mg/l was determined in an acute test (duration 24 hours) in zebra fish (Oliveira-Filho and Paumgarten, 1997). In a long term study (70 days) with snails (*Lymnaea stagnalis*) a 50 % reduction of reproduction was found at a concentration of 65 µg/l. In fish no histopathological changes or influence on growth and behaviour could be detected in long-term experiments (test concentration 800 µg/L, duration 50 days, species guppies or pellets containing 10 - 1250 mg alpha-HCH/kg, duration 3 months, species rainbow trout) (IPCS, 1992). Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions (AMAP, 2004a).

Risk characterisation
USEPA performed a dietary risk assessment for Alaskan communities for alpha and beta-HCH in 2006. USEPA estimated alpha-HCH exposures for Alaskan communities in the range of 0.00057 - 0.0039 mg/kg bw/day for adults, 0.0021 - 0.051 mg/kg bw/day for children (age 1 - 6) and 0.00073 - 0.0050 mg/kg bw/day for children (age 7 - 12). The risk is expressed as a percentage of a maximum acceptable dose or reference dose (RfD). A level of concern is reached if the dietary risk exceeds 100% RfD (USEPA, 2006). The RfD value of 0.001 mg/kg/day for chronic exposure is based on a NOAEL of 0.1 mg/kg/day (the LOAEL is 0.5 mg/kg/day) established in a subchronic toxicity study in rats and applying an uncertainty factor of 100 (USEPA, 2006). For inhalation the reference concentration (RfC) of alpha-HCH is 0.00025 mg/m^3 based on a NOAEL of 0.025 mg/m^3 for observations of liver and kidney toxicity determined in an subchronic inhalation study in rats and applying an uncertainty factor of 100 (RIVM, 2001 in USEPA, 2006).

The acute dietary exposure estimates are not of concern according to USEPA (2006). USEPA's dietary risk assessment indicates that the chronic dietary exposure estimates for alpha-HCH are above the levels of concern for high-end dietary intake estimates. The cancer dietary risk estimates for alpha-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to EPA, the risk values (% cRfD) are 57 - 390 for adult males, 67 – 460 for adult females, 210 – 5 100 for children (1 - 6 years) and 73 - 500 (7 - 12 years). The estimated cancer risk for adult males is 3.2×10^{-3} to 2.5×10^{-2} and 4.2×10^{-3} to 2.9×10^{-2} for adult females. It should be noted that these estimated incidences are at least four orders of magnitude higher than a general accepted cancer risk of 1×10^{-6}. Even though this risk estimation is very conservative due to the basic maximum detected levels it can be concluded that the dietary risks are of concern. Additionally, it has to be mentioned that the target organ of chronic toxicity is the liver and it can be expected that HCHs effects might be additive.

3   Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 55 – 80 % alpha-HCH and was used extensively worldwide as an organochlorine pesticide. Though usage of technical HCH is negligible nowadays, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles and landfills or dumping grounds. Though no quantitative estimates of these releases exist, the amounts of HCH residuals in the form of by-products from lindane production are assumed to range between 1.6 - 1.9 to 4.8 million tonnes. In addition, many sites are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of alpha-HCH facilitate long-range atmospheric transport and allow for "cold condensation" on a global scale. In addition, the low Henry's Law Constant contributes to achieve high levels in the Arctic Ocean. Moreover, it was shown that Arctic air concentrations mimicked global usage data directly until the early 1990s. Also, monitoring data from remote regions e.g. the Arctic and Antarctica suggested that detected levels, which were sometimes higher than in source regions, originate from long range transport.

Hydrolysis contributes to the overall removal of alpha-HCH in aqueous solution under alkaline pH, but under environmental conditions has minor importance. Alpha-HCH may undergo enantioselective degradation which depends on the site and medium. Reported half-life and residue analyses in soil suggest moderate persistence. However, certain environmental conditions e.g. low concentrations or low temperatures resulted in longer half-lives. Half-lives for alpha-HCH in Arctic lakes were up to 1.4 years, whereas in the Eastern Arctic Ocean enantioselective degradation resulted in a range of approximately 5 to 17 years.

Alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The BMFs as well as FWMFs in invertebrates, fish and terrestrial and marine mammals were greater than 1. Because of the individual potential to metabolize alpha-HCH, birds do not fit into this scheme. Most birds show BMFs < 1, independent of the trophic level. Especially in mammals, an enantiospecific accumulation of (+) or (-) alpha-HCH occurs (depending on the species). Combined with the lower potential for biotransformation alpha-HCH, - reaches high BMFs in mammals, with the highest concentrations in brain tissue (especially the (+) enantiomer). As all HCHs act on the central nervous system, this has to be seen with caution. To date, however, no enantiomer-specific toxicity studies for alpha-HCH are available and the reasons for the enrichment and differences are largely unclear.

Alpha-HCH has been shown to be neurotoxic, hepatotoxic, and to cause immunosuppressive effects and cancer in laboratory animals. The International Agency for Research on Cancer (IARC) has classified alpha-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that alpha-HCH might play a role in human breast cancer. Alpha-HCH is a known tumour promoting agent.

Alpha-HCH may adversely affect human health in contaminated areas as well as in Arctic regions. Based on the available toxicity data of alpha-HCH, it can be concluded that current concentrations of alpha-HCH in food and human breast milk are a matter of concern. The estimated daily intake of alpha-HCH of Arctic indigenous people exceeds safe intake reference values, even though estimation is very conservative. The dietary risks of these populations are of concern. Nevertheless it should be emphasized that traditional foods have unique social, cultural, spiritual and economic value and therefore it is strongly recommended to avoid foods in which alpha-HCH levels are of concern.

4   Concluding statement

Though most countries have banned or restricted the use of technical HCH as a pesticide, replacing it in most cases by the use of lindane, the lindane production process has produced huge amounts of HCHs residuals. The continued production and existing stockpiles of these waste isomers have been a worldwide problem and contribute to the releases into the environment.

Releases into the environment have dramatically decreased over the past 30 years, but levels in the environment suggest that alpha-HCH may persist in the environment (at lower concentrations). The cold Arctic Ocean, which is now eliminating alpha-HCH, was a sink which preserved the chemical from rapid degradation. Levels in Arctic biota do not thoroughly reflect the decreasing trend of the abiotic compartments.

Alpha-HCH is present in the terrestrial and the aquatic food chains and concentrations are a human health concern. High exposure is expected in polluted areas, which are still present around the globe. High exposure ois also possibly expected as a result of long-range transport in the Arctic region. In addition, humans and wildlife are exposed to various contaminants that can influence the toxicological effects of alpha-HCH in an additive way. Based on the inherent properties, together with estimated daily intakes of alpha-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of alpha-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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	/ logKow=3.78 BCF 　 BCF=1460 FWMF FWMFs　1 FWMF=7.2 　　　　　PCB FWMF=2.9 BMF 　　　　　　　　　　BMF 1 　betaHCH	52　　LOAEL 0.5mg/kg/day 　　　13　　NOAEL 0.1mg/kg/day 　　　　0.1mg/kg/day 　2.5mg/kg/day 12.5mg/kg/day 　　　26　　3.4mg/kg/day IARC　　　　possibly carcinogenic to human 　　　　　　　　NOAEL 0.1mg/kg/day 　20mg/kg/day	*Poecilia reticulata*　4-12 NOEC=0.032 mg/L 　- HCH 　　　　　　　　　1 2
56　(　　　) 100　　　184 　　　　　　　　　　15 　44% 　　　　　　　570 30%			

		HCH	
		30 60mg/kg/day NK	

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Programme**

Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on beta hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on beta hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/18. The text of the risk profile, as amended, is set out below. It has not been formally edited.

BETA HEXACHLOROCYCLOHEXANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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Executive summary

Mexico, being Party to the Stockholm Convention, proposed lindane as well as alpha- and beta-hexachlorocyclohexane to be included in Annex A, B or C of the Stockholm Convention. After the risk profile on lindane had already agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that beta-HCH also complied with the screening criteria laid down in Annex D of the Convention and further elaboration of the proposal and preparation of a draft risk profile should be done.

After almost forty years of extensive use worldwide, there has been a gradual replacement of technical hexachlorocyclohexane (HCH) by lindane (gamma-HCH). No significant uses of technical HCH have been reported after 2000. However releases into the environment may also occur from lindane production as well as from hazardous waste sites, landfills and contaminated sites. Because of its hazard profile and widespread abundance, technical HCH (including beta-HCH) is subject to national and international regulations and prohibitions.

Abiotic degradation processes do not play an important role in the fate of beta-HCH in the environment. Thus photolysis and hydrolysis are not significant. Under favourable conditions, beta-HCH is susceptible to biodegradation. However, compared to the gamma- and alpha-HCH, it is the most recalcitrant isomer. Laboratory and field data including a long-term soil study suggest that beta-HCH is persistent in soil, especially under low temperatures. It is mainly associated with particles and has a low leaching potential.

The physico-chemical properties of beta-HCH allow the dispersal of the substance from its sources to the Arctic mainly by long-range environmental transport via ocean currents. Beta-HCH has been detected in the Arctic Ocean and is present in marine, terrestrial species, and humans.

Beta-HCH exposure levels in local areas have declined after worldwide prohibitions and restrictions. However regions with recent exposure and/or high pollution can still show elevated levels. A special concern also arises from exposure of hazardous waste sites and dumping grounds from disposed beta-HCH residues from lindane production.

Due to its persistence, beta-HCH can still be detected at low background levels in all environmental media except in regions with recent usage and/or high pollution. Data from the abiotic environment in the Arctic are scarce, partly due to low levels compared with the other HCH isomers. In contrast to this fact, fairly high concentrations in Arctic biota including marine mammals and birds were detected with increasing levels.

Beta-HCH is present in terrestrial and aquatic food chains. Beta-HCH may bioaccumulate and biomagnify in biota and Arctic food webs, especially in upper trophic levels. In humans, accumulation in fat tissue and high concentrations in blood and breast milk may occur. Beta-HCH transfers from mothers to embryos and nursing infants.

Beta-HCH is acutely toxic to aquatic organisms and shows estrogenic effects in fish. Reduced fitness of offspring in birds as well as reduced retinol concentrations in polar bears is associated with beta-HCH and HCHs levels.

Toxicological studies with beta-HCH have demonstrated neurotoxicity and hepatotoxicity. Also, reproductive and immunosuppressive effects and effects on fertility were seen in laboratory animals. Beta-HCH has been classified in group 2B as possibly carcinogenic to humans by the International Agency on Research and Cancer (IARC). Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer.

Human exposure to beta-HCH results mostly from ingestion of contaminated plants, animals and animal products. High exposure is expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles.

Given the hazard profile and the exposure levels in the environment including the food chain, it can be concluded that beta-HCH may adversely affect wildlife and human health in contaminated and remote regions including the Arctic region. Arctic public health authorities believe the significant social, cultural and economic benefits of traditional foods outweigh the risks of contaminants such as HCH at present but give another reason for the quick control and elimination of all HCH isomers from traditional foods.

Based on the hazard profile, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

1   Introduction

During the procedure for adding lindane to Annex A of the Stockholm Convention, the POPs Review Committee discussed the proposal of lindane and concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing beta hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/8). Austria on behalf of Germany prepared the first working draft on beta-HCH.

Beta-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Beta-HCH is mainly a depressant and the final effect of the mixed isomers depends on the composition (IPCS, 2001). In general HCHs are among the most studied pesticides with respect to environmental fate and effects (Breivik et al., 1999).

1.1   Chemical Identity

Chemical name: Beta-hexachlorocyclohexane (beta-HCH)

IUPAC name: (1-alpha, 2-beta, 3-alpha, 4-beta, 5-alpha, 6-beta)-Hexachlorocyclohexane

Common synonyms: beta-1,2,3,4,5,6-Hexachlorocyclohexane; beta-Benzenehexachloride; beta-BHC, benzene-cis-hexachloride; beta-HCH; beta-Hexachlorocyclohexane; beta-Hexachlorocyclohexane; beta-isomer; beta-lindane; Hexachlorocyclohexane-Beta; trans-alpha-benzenehexachloride; beta-benzenehexachloride (Chemfinder, 2007)

CAS number: 319-85-7

Chemical formula: $C_6H_6Cl_6$

Molecular weight: 290.83

Figure 1: Structure of beta-HCH (modified from Buser et al.,1995)
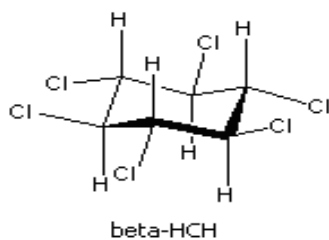
1.1.1   Physico-chemical properties

Selected physico-chemical properties of beta-HCH are provided in Table 1. Beta-HCH is more soluble in water and octanol compared to other organochlorine pesticides. Its chemical structure seems to confer the greatest physical and metabolic stability (e.g. beta-HCH has a lower vapour pressure and a higher melting point than the alpha-isomer). The physico-chemical properties (a selection is given in Table 1) of beta-HCH allow for "cold condensation", an enrichment of the substance in cold climates compared to concentrations near sources, on altitudinal and latitudinal scales described by Wania and Mackay (1996).

The Henry's Law Constant is a factor of 20 lower than for alpha-HCH and decreases significantly with water temperature which favours partitioning from air to water. Also its relatively high log K_{oa} promotes partitioning from air to environmental organic phases. This is probably one reason why transportation pathways of alpha- and beta-HCH diverge in the environment (Li and Macdonald, 2005). Based on an extensive data analysis of the physico-chemical properties of alpha-, beta- and gamma-HCH Xiao et al. (2004) concluded that its different environmental behaviour is caused by a higher solubility in water and octanol rather than the lower volatility compared to the gamma- and alpha-isomer.

Table 1: Selected physico-chemical properties of beta-HCH

Melting Point (K)	314-315 [1]
Boiling Point (K)	333 at 67 Pa [1]
Water solubility (mol*m^{-3} at 25 °C)	1.44 [2]
Vapour pressure (Pa at 25 °C)	0.053 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.037 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	8.7 [2]
Physical state	crystalline solid [1]

[1] ATSDR (2005)

[2] Xiao et al. (2004)

1.2   Conclusion of the POP Review Committee of Annex D information

The POP Review Committee evaluated the proposal regarding beta-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/8 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/16) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/10 the Committee reached the conclusion that beta-HCH meets the screening criteria specified in Annex D. The Committee also decided to establish an ad hoc working group to review the proposal further and prepare a draft risk profile in accordance with Annex E of the Convention.

1.3   Data sources

The draft risk profile is based on the following data sources:

- Proposal submitted by Mexico for listing alpha- and beta-HCH in Annexes A, B and/or C to the Convention (UNEP/POPS/POPRC2./INF/8), 2006.

- Decision POPRC-2/10 of the Review Committee, 2006.

- Information submitted by parties and observers according to Annex E of the Convention: specific and/or scientific information: Czech Republic, France, Germany, International POPs Elimination Network (IPEN), Japan, Norway, Switzerland, United States of America, general information: Algeria, Crop Life International, Kingdom of Bahrain, Mauritius, Mexico, Qatar, Republic of Lithuania and Turkey. This information is available on the Convention's website (http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/submissions.htm)

- Assessment of lindane and other hexachlorocyclohexane isomers, USEPA, 2006. http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm

- International Programme on Chemical Safety, ALPHA- and BETA-HEXACHLOROCYCLOHEXANES, Environmental Health Criteria 123, World Health Organization. Geneva, 1992. http://www.inchem.org/documents/ehc/ehc/ehc123.htm

- Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. 2006. North American Commission for Environmental Cooperation http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=2053

In addition to these information sources a literature search of public data bases was conducted. The following databases were used: ECOTOXicology database (Ecotox, http://www.epa.gov/ecotox/) Hazardous Substances Data Bank (HSDB, http://toxnet.nlm. nih.gov/cgi-bin/sis/htmlgen?HSDB), Pubmed (http://www.ncbi.nlm.nih.gov /entrez/query.fcgi?DB=pubmed), Environmental Fate Data Base (EFDB http://www.syrres. com/esc/efdb_info.htm. In general search terms include the chemical name or CAS number and/or a combination of a technical term because of the multiplicity of entries. For the same reason, specific topical and updated articles were also considered.

The reports listed above contained individual references which were not listed again in this draft risk profile. References referred to in this document are provided in UNEP/POPS/POPRC.3/INF/28.

1.4   Status of the chemical under international conventions

Beta-HCH is a constituent of technical HCH, which is regulated at least by two international agreements. The first one is the 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. Technical HCH is listed in Annex II of the protocol which restricted its use to an intermediate in chemical manufacturing only.

The second agreement is the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. HCH (mixed isomers) is subject to the PIC Procedure and is listed in Annex III of the Convention.

Canada, Mexico, and the United States signed the North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers in 2006. The goal of the NARAP is for the three member countries to cooperatively take actions to reduce the risks associated with the exposure of humans and the environment to lindane and other HCH isomers.

In the European Union the production and use of technical HCH as an intermediate in chemical manufacturing will be phased out by the end of 2007 at the latest (Regulation (EC) No 850/2004). HCHs are also one of the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the beta-isomer, are on the List of Chemicals for Priority Action under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. The objective is the prevention of pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances.

2   Summary information relevant for the risk profile

2.1   Sources

2.1.1   Production

Beta-HCH by itself is neither intentionally produced nor placed on the market. It is produced as constituent of technical HCH used as organochlorine insecticide or chemical intermediate to manufacture enriched HCH (lindane). Currently no production data on technical HCH have been reported, whereas manufacture of lindane still takes place (IHPA, 2006).

Further details on the production and reuse of HCH residuals can be found in UNEP/POPS/POPRC.2/17/Add.4 (Risk Profile on Lindane) and IHPA (2006).

The following countries which submitted information according to Annex E stated that there was currently no production or use of beta-HCH: Czech Republic, Germany, Mauritius, Mexico, Norway, Qatar, Republic of Lithuania, Turkey, Switzerland and the United States of America.

2.1.2   Trade and stockpiles

Please see section 2.1.2 of the risk profile on alpha-HCH.

2.1.3   Uses

Please see section 2.1.3 of the risk profile on alpha-HCH.

2.1.4   Releases to the environment

There are several pathways for beta-HCH for entering the environment. Historically beta-HCH was released during the manufacture of technical HCH and its use as a pesticide. Li et al. (2003) estimated global emissions of beta-HCH from the usage of technical HCH between 1945 and 2000 at 850 000 tonnes, of which 230 000 tonnes were emitted into the atmosphere over the same period. In 1980, the usage of beta-HCH was around 36 000 tonnes, and the calculated primary emissions were 9 800 tonnes (83 % attributed to the application and 17 % to soil residues due to prior applications). In 1990, figures dropped to 7 400 (usage) and 2 400 tons (emissions). In 2000, emissions of beta-HCH from soil residues were 66 tonnes in the absence of direct usage of technical HCH. Also, as a result of the ban on technical HCH in northern countries, global emissions of beta-HCH have undergone a "southward tilt" (Li et al., 2003).

Releases of beta-HCH into the environment are also possible from hazardous waste sites (USEPA, 2006), stockpiles and residues of lindane production, which are not always controlled or maintained safely (IHPA, 2006). Also, contaminated sites (e.g. from former production plants) may contribute to the environmental burden of beta-HCH (Concha-Grana et al., 2006). Germany (submitted Annex E information, 2007) reported that there are still a few isolated local sources i.e. landfills and dumps in the former GDR (East Germany) from applications of technical HCH. As a result, higher concentrations of beta-HCH in fish of the river Elbe near the former production site were detected after heavy rainfalls and floods in 2003. However, quantitative estimates of releases from hazardous waste sites and landfills are not available.

2.2 Environmental fate

2.2.1 Persistence

Investigations of the hydrolysis and photolysis of beta-HCH are extremely limited. Only one literature study regarding photodegradation has to date been available. A photodegradation half-life for a thin film of beta-HCH equal to 152 hours has been reported (ATSDR, 2005). The relevance of this result is questionable with respect to the chosen test design which does not comply with internationally accepted test guidelines on photolysis and, as pointed out by ATSDR (2005) no absorption bands were observed in the studied spectral region. In general, photolysis is not expected to be an important environmental fate process for beta-HCH since no absorption of light > 290 nm takes place.

Based on the calculated atmospheric OH rate constant of 5.73×10^{-13} cm^3/molecule-sec (HSDB, 2006) the estimated half-life is 56 days (using an average hydroxyl radical concentration of 5×10^5 molecule/cm^3 according to the TGD (2003)).

USEPA (2006) concluded that HCH isomers are resistant to abiotic processes like photolysis and hydrolysis (except at basic pH).

Beta-HCH is in principle biodegradable under oxic and anoxic conditions. However several studies have suggested that significant degradation does mainly occur under anaerobic conditions (Middeldorp et al., 1996). Degradation was observed in pure cultures, soil slurry, soil microcosm, field studies and via bioremediation techniques in the soils of contaminated sites (Phillips et al., 2005). Effectiveness of removal varied depending on the test design and environmental factors.

In general the metabolic pathway of beta-HCH occurs anaerobically via dechlorination to tetrachlorocyclohexene and dichlorocyclohexadiene, an unstable metabolite. Chlorobenzene and benzene were formed as stable end products under methanogenic conditions. These metabolites can be further aerobically or anaerobically mineralised (Phillips et al., 2005). Compared to other HCH isomers laboratory data using radio-labelled beta-HCH have shown only minimal and incomplete mineralization (Sahu et al., 1995).

Beta-HCH is considered to be the most recalcitrant isomer due to its chemical structure (Decision POPRC-2/10, 2006). Under favourable laboratory conditions several strains of bacteria e.g. *Bacillus brevis*, *Bacillus circulans*, *Dehalobacter sp.* in conjuction with *Sedimentibacter sp.,* isolated from HCH polluted sites, have been identified as beta-HCH degraders (Gupta et al., 2000; van Doesburg et al., 2005). But only a few e.g. *Sphingobium sp.* were able to transform beta-HCH under aerobic conditions (Sharma et al., 2006).

Research on the intrinsic stimulation and additives for soil bioremediation of beta-HCH polluted sites is under way (e.g. Kumar et al., 2005; MacRae et al., 1984) but to remove the isomer remains a difficult challenge (Phillips et al., 2005). Regarding the effects on the intrinsic soil microbial population of an uncontaminated soil, Bhatt et al. (2006) showed that the application of technical HCH disturbed the microbial community irreversibly.

In general, climatic conditions as well as soil texture and organic matter altering substance sorption, water content, pH and bacterial growth influence degradation rates (IPCS, 1992). Phillips et al. (2005) stated that bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported.

Data on laboratory soil studies or field investigations are limited. Singh et al. (1991) reported half-lives of 100 and 184 days on cropped and uncropped plots respectively, in a sandy loam in India under subtropical conditions. The applied formulated HCH was immediately incorporated into the top layer of the soil. Soil samples were taken randomly from the plots in 0-15 cm depths. No quantitative information on losses of beta-HCH by volatilisation or leaching during the experiment is available in the citied study. In a temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil no degradation of beta-HCH under anaerobic conditions. Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 44 % of the beta-HCH isomer after 15 years in a sandy loam in Canada. Approximately 30 % of beta-HCH (from applied technical HCH) was observed after 570 days in a field test in Japan on agricultural field plots (Suzuki et al., 1975). Also, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, beta-HCH was found in concentrations which are more than one order of magnitude higher compared to the other isomers. Volatilisation from soil surfaces is considered not to be an important fate process (HSDB, 2006; Singh et al., 1991).

Beta-HCH was stable in a sediment/water study under laboratory conditions. In addition, isomerisation of alpha- to the beta-HCH isomer was observed (Wu et al., 1997). Detailed information regarding isomerisation can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4). Levels of the beta-HCH isomer compared to alpha-, gamma- and delta-HCH were highest in porewater (1 423 ng/l) compared to concentrations in surface water (92.5 ng/l) and sediment (3.9 ng/g) of the Minjiang River Estuary, China (Zhang et al., 2003). No degradation half-lives in water or sediment are available, however, based on monitoring studies, it can be assumed that beta-HCH is persistent and does not undergo degradation easily.

2.2.2   Bioaccumulation

The octanol-water partition coefficient (log K_{ow} = 3.78) for beta-HCH indicates that it has a potential to bioaccumulate, especially in combination with its shown persistence in animal tissue (Walker et al., 1999),

The BCF according to the former OECD test guideline 305 E in zebra fish was equal to 1 460, which was the highest BCF (whole body) compared to determined values for alpha- (1 100) and gamma-HCH (850) (Butte et al., 1991). According to the ECOTOX database this was also the highest reported BCF. Nonetheless, the screening criteria were considered fulfilled by POPRC for beta-HCH as set out in the evaluation contained in the annex to its decision POPRC-2/10.

Several studies suggest that the relative proportions of HCH isomers vary dramatically across species in the Arctic marine food web (USEPA, 2006). Concentrations of beta-HCH increased with the trophic level especially in upper trophic levels (marine mammals) (USEPA, 2006; Hoekstra et al., 2003). Whereas it is assumed that organochlorine (OC) profiles in mammals are mainly influenced by their ability to biotransform and excrete OCs, high detected levels of beta-HCH in various mammalian species are another indication of its recalcitrant nature and slow elimination. Hop et al. (2002) showed that beta-HCH biomagnifies differently in poikilotherms and homeotherms. Beta-HCH increased more among homeotherms (birds and mammals) with the trophic level. Fisk et al. (2001) reported the highest BMF (biomagnification factor) in birds compared to the other trophic levels, but migration and prey items are also considered to influence the variability of the BMFs. These data are in line with findings from Moisy et al. (2001). In general, studies from Arctic marine food webs show that BMFs for nearly all examined species as well as obtained food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, are greater than 1. For example Fisk et al. (2001) reported a FWMF of 7.2 which is comparable to higher chlorinated PCBs. A FWMF of 2.9 was calculated by Hoekstra et al. (2003) for the marine food web in the Beaufort-Chukchi Sea. However in sub-Arctic waters e.g. the White Sea, values for for beta-HCH were lower compared to the other food web studies. Differences in feeding habits and availability/levels of contaminants were suggested as being responsible by Muir et al. (2003).

Also, in the terrestrial food chain, beta-HCH may biomagnify. Data obtained from an investigation in south India showed that HCHs were the predominant OCs in biota. Elevated concentrations were measured in snails and subsequently their predators (e.g. little egret) showed BMFs above 1 (Senthilkumar et al., 2001). Also Wang et al. (2006) found beta-HCH as a major compound in mollusks (submitted Annex E information by IPEN, 2007).

Kelly at al. (2007) have recently shown that, for substances with a logKoa >6 and a logKow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is well illustrated by beta-HCH, in the marine mammalian and terrestrial food webs, as such compounds biomagnify strongly up to 3000- and 400-fold respectively.

 Fish, marine and terrestrial mammals as well as birds are the major nutrition sources of several human Arctic population groups and thus exposure through diet is much more likely than for most populations in the developed world. Levels of beta-HCH in breast milk among women from indigenous people on the Chukotka Peninsula, Russia (Chukotsky rayon, mean value 370 ng/g lipids) are highest compared to other northern towns of Russia and to levels in Canada (Nunavik, by 30 times; AMAP, 2004). Also, concentrations of maternal blood sampled between 1994 and 1997 were highest in Russian mothers (Arctic non-indigenous population, serum concentration 223 µg/kg lipid), but elevated levels were also found in Iceland (23 µg/kg) and in the Canadian Arctic (AMAP, 2003).

2.2.3   Long-range environmental transport

Many studies and monitoring data have detected beta-HCH regularly in the Arctic environment as well as in biota (e.g. AMAP, 2004; AMAP, 2003). Because technical HCH, including beta-HCH, was never extensively used in this remote area, this is evidence of its long range transport (UNEP/POPS/POPRC.2/17/Add.4).

Based on monitoring data from Arctic air, beta-HCH appears to be less subject to direct atmospheric loading into the high Arctic. This can possibly be explained by differences in the Henry's Law Constant and the air/octanol partition coefficient that show enhanced affinity to organic matter (Li et al., 2002). Thus rain scavenging is much more efficient for beta- than for alpha-HCH and besides, the frequency of precipitation is considerably higher in the North Pacific compared to the Arctic. This suggests that beta-HCH enters the Arctic probably by mechanisms involving wet deposition or partitioning into the North Pacific surface water and subsequently entering the Arctic in ocean currents passing through the Bering Strait (Li et al., 2003). The Bering and Chukchi Seas are the most vulnerable locations for beta-HCH loadings (Li et al., 2002). Concentrations of beta-HCH around the Bering Strait in the 1990s reached approximately 1.2 ng/l (Li and Macdonald, 2005). Thus "cold condensation" also occurred for beta-HCH, but mainly in the Pacific Ocean and Bering Sea upstream of the Arctic Ocean. Thus beta-HCH reached the Artic later compared to alpha-HCH and differed in its spatial distribution (Li et al., 2002). This spatial and temporal distribution is also reflected in residue levels in marine and terrestrial mammals as well as in local residents (Li and Macdonald, 2005).

Measurement of beta-HCH in high mountains in the Czech Republic is another proof for its long-range transport potential (submitted Annex E information by the Czech Republic, 2007).

According to model calculations with the OECD Pov and LRTP Screening Tool beta-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and OCs (Wegmann et al., 2007). Model input properties of the chemicals include partition coefficients in air-water and octanol-water as well as half-lives in air, water and soil and the Henry's Law constant (based on figures contained in UNEP/POPS/POPRC2./INF/8). The model considers all environmental compartments quantitatively. The results of the model do not indicate absolute levels in the environment but help to compare possible POPs with identified POPs (reference chemicals: PCB congeners 28, 101, 180, HCB, carbon tetrachloride and alpha-HCH) according to their environmental persistence and potential for long range transport. Uncertainties in the chemical properties were investigated by Monte Carlo uncertainty analysis.

2.3   Exposure

Direct exposure to beta-HCH resulted from the production (including manufacture of lindane) and use of technical HCH. Because of the persistence, high exposure is also expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles. Though usage of technical HCH has practically ceased worldwide monitoring data based on the ratio of the alpha/gamma-isomer still suggest possible releases of technical HCH in certain areas (Zhang et al. 2003; Qian et al., 2006; Zhulidov et al., 2000).

Exposure of the general public results mostly from the ingestion of contaminated plants, animals and animal products. Inhalation of ambient air and consumption of drinking water are further sources of exposure, although to a minor extent. Intake through indoor air may be considerable for people living in houses treated for pest-control purposes. Infants may be exposed during fetal development and breastfeeding.

2.3.1   Environmental monitoring data from local areas

Generally environmental levels in local areas have dropped after restrictions and prohibitions of the usage of technical HCH (IPCS, 1992). However, monitoring data show its ubiquitous distribution in all environmental media. For example, beta-HCH (up to 15 µg/kg dry substance) has been detected using passive monitoring in lichens in various locations (e.g. cities, industry, rural) in Switzerland (submitted Annex E information by Switzerland, 2007). Also, a recently (2004) performed monitoring programme in Japan revealed that beta-HCH had been detected in all specimens. The reported values (range) are as follows: water 0.031-3.4 ng/l, sediment 0.004-53 ng/g dry weight, shellfish 0.22-1.8 ng/g wet weight, fish trace-1.1 ng/g wet weight, bird 1.1-4.8 ng/g wet weight, air (warm and cold season) 0.53-110 pg/m^3 and 0.32-78 pg/m^3 (submitted Annex E information by Japan, 2007). The Czech Republic (Annex E information, 2007) reported that, with regard to HCHs, the most severe situation is in central and southern Moravia, where sediment particles are found in amounts of tens of ng/g and in some cases even in hundreds of ng/g (no information on which basis the concentrations are expressed was submitted).

However, heavily contaminated soils were found in the proximity of sources. HCH concentrations of 40 - 225 mg/kg were found in the topsoil around a chemical plant in Albania. Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, while Russian soils near the Lena River contained 0.001-0.017 mg/kg HCH (UNEP, 2003).

Compared to the other HCH isomers, concentrations of beta-HCH in the air are low. Elevated levels were detected in higher mountains (Mount Everest Region) of 11.2 pg/m^3 compared to up to 1 pg/m^3 in the Arctic (Li et al., 2006). Seasonal changes in beta-HCH concentrations in Japan (mean 23 pg/m^3) in 2000 were probably caused by re-emissions from a terrestrial source (Murayama et al., 2003). Unlike alpha- and gamma-HCH observed concentrations of beta-HCH in air at most locations near the Great Lakes in North America did not show significant trends between 1990 and 2003. The highest concentration was observed in Chicago with a maximum of 73 pg/m^3 (mean 12 pg/m^3, 1999-2003, gas phase, Sun et al., 2006a). Regarding the occurrence of beta-HCH in precipitation samples from the same region (mean concentrations 0.16 - 0.64 ng/l) a significant increase in concentrations at three Great Lakes stations over the last decade was observed (Sun et al., 2006b).

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. For example, concentrations of HCHs (mainly the beta-isomer) in one fish species (*Java tilapia*) from India amounted to up to 2 000 ng/g wet weight (Senthilkumar et al., 2001). Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of beta-HCH of 1.5 ng/g wet weights (UNEP, 2003). Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998).

A global sampling study of free-range chicken eggs found that of 30 egg samples taken from 17 different geographic locations, beta-HCH was detected in all samples. Levels were particularly high in samples taken in Senegal and India. (Blake, 2005).

Birds and bats can accumulate higher concentrations of beta-HCH. According to submitted Annex E information by Norway (2007) Bustnes et al. (2006) concluded that beta-HCH levels in blood and eggs were higher in the endangered subspecies compared with the increasing subspecies of the black-backed gulls in Norway. One explanation might be the migration route through the Black Sea where HCH levels are considerable high.

In a study of resident and migratory birds collected from South India, the organochlorine contamination pattern varied depending on the migratory behaviour. Resident birds living in the same region for their entire life span contained relatively greater concentrations of HCHs (14-8800 ng/g wet weight). Long distance migratory birds which have their breeding grounds in Europe, Russia, the Middle East, Papua New Guinea and Australia contained HCHs at levels of 19-5500 ng/g. Among various HCH isomers, beta-HCH was the predominant contaminant in all the bird species (UNEP, 2003). Similar levels were reported in a later investigation (Senthilkumar et al., 2001) including residue levels of HCHs in egg yolks (range 350-49000 ng/g fat weight). Again beta-HCH was the predominant isomer in birds (no detailed values for beta-HCH were reported). In addition, HCHs concentrations (mainly the beta-isomer, up to 330 ng/g wet weight) in Indian bats were investigated, which were higher in 1998 than in 1995 and highest compared to other parts of the world.

A local source of beta-HCH was the usage of technical HCH in the Russian north against nuisance insects on domesticated reindeer by indigenous human populations (Li et al., 2004). However, no quantitative estimates of these exposure levels exist.

2.3.2   Exposure as a result of long-range environmental transport

The main transportation pathway of beta-HCH to the Arctic is assumed to be ocean currents (Li et al., 2002). Compared to levels of alpha-HCH in sea water, beta-HCH levels were lower - partly due to reduced emissions and different spatial and temporal distributions, e.g. beta-HCH reached its peak (approximately 0.3 ng/l) in the north American Arctic Ocean in 1994, around 10 years after the alpha-HCH levels had reached their peak. Enrichment of the upper waters of the North Pacific Ocean and Bering Sea (approximately 1.3 ng/l 1988-1999) caused higher concentrations in the Chukchi Sea and subsequent decreases towards the Arctic interior ocean (Li and Macdonald, 2005). Data on beta-HCH from surface water of the Canadian Archipelago in 1999 showed concentrations of 0.1 ng/l (Bidleman et al., 2007).

This spatial distribution is also reflected in the levels in biota. Hoekstra et al. (2002) found that bowhead whales exhibit a reversal in their blubber alpha-/beta-HCH ratios on their migration route between the Bering to the Beaufort Sea. Also elevated residues of HCH isomers in marine mammals of the Canadian Archipelago are likely due to the high concentrations of HCH isomers in the water because HCH isomers are the most abundant organochlorines in the Arctic Ocean (NARAP, 2006).

Beta-HCH is not so abundant in the Arctic abiotic environment and therefore it has not been studied as well as the other HCH isomers. Measured levels in the Arctic air (e.g. < 1 pg/m^3 from six Arctic circumpolar located sites between 2000-2003, Su et al. (2006)) and in terrestrial as well as freshwater ecosystems were low (AMAP, 2004). HCHs also show a high degree of spatial variability in the levels of contamination across the Russian north (AMAP, 2004).

Levels in the Arctic terrestrial environment (including carnivores) are much lower than in the marine compartment and its predators. However, beta-HCH has been detected in the fat of male Arctic foxes (up to 810 ng/g wet weight) in Alaska (AMAP, 2004). The highest levels of HCH in polar bears were detected in the Beaufort Sea population (approx. 770 ng/g wet weight in fat). Beta-HCH accounted for 93 % of HCH residues.

The metabolism of beta-HCH is very limited in Arctic seabirds, and therefore beta-HCH is detected more readily than alpha- and gamma-HCH. But concentrations vary notably between species, depending on the trophic position and migration. Higher levels of beta-HCH were observed in the North American Arctic in closer proximity to Asia where HCH was recently used. Levels were below 1 ng/g in bird tissue and 30 ng/g wet weight in eggs (AMAP, 2004).

Regarding temporal trends, it was shown that beta-HCH levels in seabirds, ringed seals and polar bears increased, whereas belugas showed no difference from 1982 to 1997 (AMAP, 2004).

2.3.3   Food

Daily intake values of beta HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be below 0.001 µg/kg /day The average concentration of beta-HCH in 234 ready-to-eat foods was 0.0027 µg/kg (no information on which basis the concentrations are expressed, ATSDR, 2005). In the Total Diet Study conducted by USFDA in 2003 on 100 food items, beta-HCH was detected in 12 items (submitted Annex E information by IPEN, 2007). In the USA, the average daily intake of beta-HCH was <0.1-0.4 ng/kg body weight (bw) (depending on age) during the years 1982-1984 and was generally below 0.1 ng/kg bw during the years 1986-1991 (ATSDR, 2005). In a total diet study from Canada (1993-1996), an average daily dietary intake of 0.39 ng/kg bw beta-HCH was reported (EFSA, 2005). In fat-containing food products, levels ranged up to 0.03 mg/kg (fat) but in milk products levels up to 4 mg/kg (fat) were detected (WHO, 2003). In the United States and Canada levels in food are slowly decreasing. Within the European countries representative dietary intake studies are scarce. One was performed

in the Czech Republic. The median intake values for beta-HCH declined from 8.4 ng/kg bw in 1994 to 2.1 ng/kg bw in 2002 (EFSA, 2005). A local diet study from Spain showed elevated daily intakes of 0.1 µg beta-HCH (Urieta et al., 1996). Fish and clam samples from India contained 0.001 and 0.02 mg beta-HCH/kg wet weight respectively (Nair and Pillai, 1992). Because of the global trade of foodstuffs, feed ingredients and food products from regions with ongoing or recent use of HCHs, which are supposedly more contaminated, might be imported by countries where technical HCH has already been phased out.

High levels of beta-HCH levels in food are documented for the Arctic Region (AMAP, 2004). Subsistence foods in Alaskan communities from the years 1990 to 2001 were analysed for total HCH in order to estimate dietary intakes by indigenous people. Highest concentrations were found in marine mammals of whale (391 ng/g) and seal (215 ng/g). High concentrations were documented for walrus (20 ng/g), whitefish (20 ng/g) and salmon (26 ng/g). Berries contained 10 ng/g and ducks 7 ng/g (no specification if values referring to whole body or lipid basis reported) (USEPA, 2006).

2.3.4   Body burden

2.3.4.1 General population

Beta-HCH is the most prevalent HCH-isomer in human fatty tissue. The half-life of beta-HCH after inhalation exposure in the body is 7.2-7.6 years (ATSDR, 2005). Human biomonitoring studies in the United States showed that median levels of beta HCH in post-mortem human adipose tissue samples decreased over time (0.45 ppm in 1970 to 0.16 ppm since 1981) (ATSDR, 2005).

A comparison between body compartments showed median levels of 0.13 ng/g in whole blood and 18 ng/g in adipose tissue (ATSDR, 2005). According to the results of the National Reports on Human Exposure to Environmental Chemicals, beta-HCH serum concentrations in the US population have been declining since 1970. For all tested age groups (12 years and older), the 95th percentile of beta-HCH serum concentrations on a lipid-weight basis decreased from 68.9 in the years 1999-2000 to 43.3 ng/g in the years 2001-2002. Concentration levels (2001/2002) in females were higher (54.5 ng/g) than in males (29.2 ng/g). Highest concentration levels were found in the Mexican Americans (84.4 ng/g). Comparably low levels were found in the age group 12-19 years (8.44 ng/g) (CDC, 2005). Age-related increases in the levels of beta-HCH have been observed in several studies and documented by the German Commission on Biological Monitoring (Ewers et al., 1999).

Comparably high concentrations were detected in human blood serum samples from Romania. Beta-HCH was detected in all samples (n = 142) with a median concentration of 923 ng/g lipid (range 38-11690 ng/g) (Dirtu et al., 2006). High concentrations were reported for India due to agricultural use and Malaria control activities. Blood serum samples from India contained up to 0.02 mg beta-HCH/l, whereas adipose tissue contained up to 0.18 mg/kg (Nair and Pillai, 1992).

2.3.4.2 Indigenous population

Beta-HCH concentrations in blood plasma samples from different regions and ethnic groups of indigenous mothers of the Arctic were 0.04 - 0.11 µg/l (Canada), 0.07-0.56 µg/l (Greenland), 0.12 - 0.53 µg/l (Alaska), 0.31 - 3.1 µg/l Russian Arctic (maximum level: 11.6 µg/l), 0.16 - 0.21 µg/l (Iceland), 0.05 - 0.09 µg/l (Norway, Finland and Sweden) and 0.11 µg/l from the Faroe Islands (AMAP 2004, values given as geometric means, with the exception of Alaska which are given as arithmetic means). The highest concentrations in blood samples of the indigenous population were reported for the Russian Arctic.

Comparative investigations of the maternal blood and cord blood of indigenous mothers for beta-HCH in the Russian Arctic were highly dependent on the residential area. The mothers with the highest exposure (Chutkotsky District) had blood concentrations (µg/l plasma, geometric mean and range) of 2.0 (0.6 - 7.6) µg/l whereas the cord blood contained 0.8 (n.d.- 8.0) µg/l (AMAP, 2004:2). The variation in body burden for indigenous people may also be due to local sources in addition to variations in consumption of local marine foods (AMAP, 2004:2).

2.3.5   Exposure of children

Children are at specific developmental stages more vulnerable against chemical substances than adults. It is not known if children are more susceptible than adults to health effects from exposure to beta-HCH. Placental transfer of HCH in humans has been well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Beta-HCH is lipophilic and accumulates in adipose tissue and breast milk. This is another relevant exposure source for children (USEPA, 2000). Several studies concerning beta-HCH in breast milk are listed in Table 2. It could be shown, that due to restrictions of use, concentrations are constantly declining.

It can be concluded that beta-HCH concentrations in breast milk are highly exposure-dependent. Whereas in some areas concentrations are very low, i.e. 13 ng/g in Poland, in other areas i.e. Russia, Ukraine, Romania they are very high (up to > 800 ng/g). In general it can be expected that in several East European and developing countries concentrations

are still very high. Especially high concentrations were reported for India and China (Wong et al., 2002). Extremely high levels were also reported for cotton pickers in Pakistan (UNEP, 2003).

Due to bioaccumulation in the Arctic marine food web, high concentrations were found in the breast milk of indigenous mothers of Arctic regions.

Table 2. Concentrations of beta HCH in breast milk

Country/region	Levels (lipid weight basis)	Comments	References	Year
Germany	0.12 mg/kg	Start of Monitoring program 1984	Fürst et al. in EFSA, 2005	1984
Germany	0.02 mg/kg	Continuous Monitoring since 1984	Fürst et al. in EFSA, 2005	2001
Spain	0.24 µg/g	51 samples	Hernandez et al. in Wong, 2002	1991
Canada	0.6-0.8ng/g	Lower concentration: population near Great lakes	Mes and Malcolm in ATDSR, 2005	1992
Canada	0,02 µg/g	497 samples	Newsome and Ryan in Wong, 2002	1992
Brazil	0.27 µg/g	40 samples	Paumgartten et al. in Wong, 2002	1992
Russia Murmansk	853 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Russia Nonchegorsk	740 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Ukraine	731 ng/g	200 samples	Gladen et a.l in Dirtu, 2006	1993-1994
Czech Republic	71 ng/g	17 samples	Schoula et al. in Dirtu, 2006	1993-1994
Kazakstan	2.21µg/g	33-76 samples	Hooper et al., in Won, 2002	1994
Siberian Russia	40 -142 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Klopov et al. 1998, 2000 in AMAP 2004	1994-1995
Northern Russia	120 -401 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Polder et al. in AMAP 2004	1994-1995
Australia	0.35µg/kg	60 samples	Quinsey et al in Wong, 2002	1995
Afrika, Uganda,	0.005-0.25 mg/kg	-	Ejobi et al. in ATDSR, 2005	1996
India	8.83 µg/kg	Delhi, Age group: 20-30 61 samples	Banerjee et al. in Wong, 2002	1997
India	0.022 – 0,078 mg/kg	Region under Malaria control	Dua et al. in ATDSR, 2005	1997
Pakistan	0 – 0.90 mg/kg	Cotton pickers	Masud and Parveen, 1998 in UNEP, 2003	1998
Nairobi, Kenya	0.0830-0.026 mg/kg	Urban population	Kinyamu et al.	1998
Japan, Osaka,	5.43 µg/g	Estimated use in Japan: 400 000 tons	Konishi et al. 2001	1972
Japan, Osaka,	0.21 µg/g	Ban of organochlorine compounds in 1970ies	Konishi et al. 2001	1998
Romania, Iassay	640 ng/g	19 samples	Covaci et al. in Dirtu, 2006	2000
Czech Republic	56 ng/g	43 samples	Cajka and Hajslova in Dirtu, 2006	2000
China, Hong Kong	15.96 µg/g	Uncontrolled agricultural use	Wong et al. 2002	1985
China, Hong Kong	0.95 µg/g	115 samples	Wong et al. 2002	1999
China, Guangzhou	1.11 µg/g	54 samples	Wong et al. 2002	2000
Turkey	149 ng/g	37 samples	Erdoorul et al. in Dirtu, 2006	2003
Poland	13 ng/g	22 samples	Jaraczewska et al. in Dirtu, 2006	2004
Sweden, Copenhagen	13.64/12.29 ng/g	Cases/Controls Cryptorchidism- study	Daamgard et al.	2006

2.3.6   Information on Bioavailability

Beta-HCH is moderately associated with organic matter in the environment. Uptake by plants and residues in vegetation as well as by food and feed is well documented (Willet et al. 1998; ATSDR, 2005; EFSA, 2005). Though beta-HCH is not assumed to be very mobile in soil there have been cases of groundwater contamination in the past (HSDB, 2006).

In biota, beta-HCH is selectively accumulated in certain tissues (e.g. liver, muscle, fat) and affects several organs (Willett et al., 1998). It can be concluded that beta-HCH is bioavailable in the environment and in biota.

2.4   Hazard assessment for endpoints of concern

2.4.1   Human Health

Information on the toxicity of beta-HCH is mostly derived from experimental studies in animals. Compared to lindane, the data available are limited, especially concerning human data because occupational exposure occurs mainly with technical-grade HCH and lindane.

Studies of acute/short-term toxicity via the oral route, subchronic and chronic oral toxicity studies and a limited number of studies of reproductive effects are available. No studies of the toxicity of beta HCH via inhalation and dermal application have been conducted. There is a lack of dose-response data after oral exposure in all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For further studies and details the more comprehensive toxicological profiles should be consulted (IPCS, 1992; ATDSR, 2005; USEPA, 2006).

*Acute Toxicity/ Neurotoxicity:*The concentration range for lethal acute toxic effects is - according to IPCS (1992) - 150 mg/kg to > 16000 mg/kg in mice and 600 mg/kg to > 8000 mg/kg in rats. Symptoms of acute toxicity affect mainly the nervous system: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions and cramps.

*Subchronic toxicity:*In a 13-week study in rats, the effects of oral exposure to beta-HCH (0, 2, 10, 50, 250 mg/kg diet) were investigated. In all dose groups, liver effects were observed. At the highest dose tested (250 mg/kg diet) half of the animals died following ataxia, progressive inactivity, and coma. Observed effects included growth inhibition, decrease of red and white blood cells, increase of liver enzymes and liver effects (increase in organ weight, centrilobular hepatocytic hypertrophy). A decrease in thymus weight (50 and 250 mg/kg) and atrophy of the testes were observed. The females showed atrophy of the ovaries with impaired oogenesis and focal hyperplasiea as well as metaplastic changes of the endometrial epithelium, which was interpreted as a possible estrogenic action of beta-HCH (van Velsen et al., 1986). A NOAEL of 2 mg/kg diet (equivalent to 0.1 mg/kg bw/day) was established (IPCS, 1992; EFSA, 2005).

Chronic Toxicity: A long-term study (52 weeks) in rats with 0, 10, 100 and 800 mg/kg beta-HCH in their diet (i.e. 0.5, 5 and 40 mg/kg bw/day) led to liver enlargement and histological changes. Nearly all animals died. The LOAEL was 10 mg/kg diet (Fitzhugh et al., 1950).

A two-generation reproduction study of rats exposed to 10 mg/kg diet resulted in increased mortality and infertility. The NOAEL was 2 mg beta-HCH/kg diet (equivalent to 0.1 mg/kg bw/day) (van Velsen in IPCS, 1992).

Genotoxicity: Beta-HCH was not mutagenic to bacteria (*Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537) with and without metabolic activation and did not induce DNA damage in bacteria. Positive results were seen in an in-vivo rat bone marrow chromosomal aberration study (EFSA, 2005).

Carcinogenicity: Studies of the carcinogenicity of beta-HCH are limited. Several studies in mice were performed, but their value is limited. On the one hand their duration, due to high mortality, was too short; on the other hand histopathological evaluations were missing. Studies in rats have been inadequate due to high mortality and small animal numbers. One study in mice is adequate for an evaluation of the carcinogenicity of beta-HCH. 200 mg/kg beta-HCH in the diet (equivalent to 40 mg/kg bw/day) for 110 weeks led to liver enlargement, hyperplastic changes and an increase in benign and malignant tumours in the exposed mice. In a 32 weeks study where 0, 100, 300, 600 mg/ per kg diet were given to mice, liver toxicity and atypical proliferation was observed in all dose groups (IPCS, 1992). In a 24-week study in mice - given 0, 50, 100, 200, 500 mg beta-HCH /kg diet - liver tumours and nodular hyperplasia in the highest dose group was observed (IPCS, 1992). In a 26-month study, liver cancer in mice was observed at a daily dose of 34 mg/kg (ATSDR, 2005). Based on these data beta-HCH has been classified as possible human carcinogen by IRIS (Integrated Risk Information System). Studies on the mode of action of carcinogenicity showed no clear initiating potential of beta-HCH. In one study the hepatocarcinogenic action of beta-HCH was shown with PCBs as promoting agent (ATSDR, 2005).It was suggested that the neo-plastic response observed with beta-HCH most likely occurs due to a non-genotoxic mechanism (IPCS, 1992). Beta-HCH has been shown to have tumour-promoting activity.

The International Agency for Research on Cancer (IARC) classified beta- HCH in group 2B: limited evidence for carcinogenicity. A positive association has been observed between exposure to beta-HCH and cancer, for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence. USEPA has classified technical HCH and alpha-HCH as probable human carcinogens and beta-HCH as a possible human carcinogen (ATSDR, 2005). The US Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Endocrine mediated toxicity: Degenerative changes in male reproductive tissues and sperm abnormalities in rats and mice were described (ATSDR, 2005). In a 13-week study, 0, 50, 150 mg beta-HCH/kg diet were given to Wistar rats. At 150 mg/kg diet, atrophy of the testes in males and increase in uterine weights in females and significantly reduced weight gains were reported (IPCS, 1992). Several other studies showed effects such as decrease in sperm counts and sperm abnormalities as well as histological effects on the testes and uterus at high doses of beta-HCH exposure (USEPA, 2006).

Animal studies and a study with MCF-7 cells showed weak estrogenic effects of beta-HCH.

Reproductive toxicity: Adverse reproductive effects after beta-HCH treatment have been observed in laboratory rodents and minks (ovarian atrophy, increased length of estrous cycle, disruption of ovarian cycling, decreased ovulation rate in female, and a decrease in the number of sperm and/or spermatids, degeneration of seminiferous tubules and testicular atrophy in male animals). Also embryotoxic effects were observed (ATSDR, 2005).

Beta-HCH has been shown to increase fetal deaths within 5 days of birth at a dose of 20 mg/kg/day given to rat dams (USEPA, 2006).

Immunotoxicity: Mice, treated with beta-HCH (60 mg/kg/day) orally for 30 days showed decreased lymphoproliferative responses to T-cell mitogens and decreased natural killer cytolytic activity. The NOAEL was 20 mg/kg/day (USEPA, 2006). Cortical atrophy of the thymus was observed at a dose of 22.5-25 mg/kg/day (van Velsen et al., 1986).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported in workers exposed to technical HCH during pesticide or fertilizer formulation. Although beta-HCH is only a minor component of technical-grade HCH, it reached higher levels and persisted longer in the serum than either alpha- or gamma-HCH. 60-100 % of the total HCH measured in serum was beta-HCH (0.07-0.72 ppm). Workers suffered from paresthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme levels were enhanced as well as IgM (ATSDR, 2005). Inhalation of HCH (mixed isomers may lead to irritation of the nose and throat (IPCS, 2006). The observation of serious hepatic effects in animals (e.g., fatty degeneration and necrosis) suggests that the same results could potentially occur in workers following prolonged occupational exposure.

Beta-HCH levels were higher in the blood of women with miscarriages compared to a control group. Several other organochlorine pesticides were also higher in these women, and therefore it was not possible to establish a causal relationship (Gerhard, 1999).

A possible link between human exposure to HCH and breast cancer has been examined in several epidemiological studies. Most studies showed a weak - not statistically significant - correlation. A non-significant trend between beta-HCH in serum and cancer risk was observed during a 17-year follow-up of a Copenhagen cohort study (Hoyer et al., 1998). Blood levels of beta- HCH were higher in women with breast cancer (in the 31-50 age group) when compared to women without breast cancer (Mathur et al., 2002). In one Chinese study (article in chinese) a significant association between high beta-HCH concentrations in blood and breast cancer in premenopausal women was observed (Li et al., 2006).

In another study a possible association between breast milk concentrations of various organochlorine pesticides including beta-HCH and cryptorchidism was investigated. Beta-HCH was measurable, but not statistically significantly higher in case milk than in control milk. A combined statistical analysis of the eight most abundant persistent pesticides, including beta-HCH, showed that pesticide levels in breast milk were significantly higher in boys with cryptorchidism (Damgaard et al., 2006).

2.4.1.1 Risk characterisation

In 2006 the United States Environmental Protection Agency (USEPA) performed a risk assessment that indicated potential risks from dietary exposure to the alpha and beta HCH isomers to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The dietary profile (intake rates) is based on the subsistence food harvest amounts of nearly 180 communities from the Community Profile Database Version 3.11 dated 3/27/01 from the Alaska Department of Fish and Game Division of Subsistence (data from 1990 to 2001, USEPA, 2006).

USEPA estimated beta-HCH exposures for Alaskan communities in the range of 0.00043-0.0032 mg/kg bw/day for female adults, 0.0014-0.010 mg/kg bw/day for children (age 1-6) and 0.00048-0.0036 mg/kg bw/day for children (age 7-12). The risk is expressed as a percentage of a maximum acceptable dose or reference dose (RfD). A level of concern is reached if the dietary risk exceeds 100 % RfD. The RfD for acute oral toxicity is 0.05 mg/kg/day. The RfD value for intermediate duration is based on a LOAEL of 0.18 mg/kg/day established in a subchronic study in rats and applying an uncertainty factor of 300 (ATSDR, 2005). On this basis USEPA established a chronic RfD of 0.00006 mg/kg/day by assessing another uncertainty factor of 10 for chronic exposure. RIVM calculated a chronic oral RfD of 0.00002 mg/kg/day for beta-HCH based on a NOAEL of 0.02mg/kg/day for observations of infertility in two semi-chronic oral studies on reproduction in rats and applying an uncertainty factor of 1000 (RIVM, 2001 in USEPA, 2006).

Levels of concern are reached if the dietary risk exceeds 100 % RfD. The acute dietary exposure estimates are not of concern according to USEPA (2006). USEPA's dietary risk assessment indicates that the chronic dietary exposure estimates for beta-HCH are above the levels of concern for both low and high end dietary intake estimates. The cancer dietary risk estimates for beta-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to USEPA, the risk values (% cRfD) are 620-4700 for adult males, 720-5300 for adult females, 2 300-17 000 for children (1-6 years) and 800-6000 (7-12 years). The estimated cancer risk for adult males is 6.7×10^{-4} to 5.0×10^{-3} and 7.7×10^{-4} to 5.8×10^{-3} for adult females respectively. It should be noted that a general accepted cancer risk is 1×10^{-6}. Even though this risk estimation is very conservative due to the basic maximum detected levels it can be concluded that the dietary risks are of concern. Additionally, it has to be mentioned that the target organ of chronic toxicity is the liver and it can be expected that HCHs effects might be additive. It has to be considered that the RfD based on effects on fertility (RIVM, 2001 in USEPA, 2006) is remarkably lower and would be exceeded to an even greater extent.

As beta-HCH is present in cord blood and breast milk infants may be exposed to the damaging reproductive effects of HCH inside and outside the womb (USEPA, 2000).

Also, based on the study of Nair et al. (1996), levels of 0.198 mg beta-HCH/l in breast milk would lead to an intake of 0.1386 mg/l (700 ml intake) which is almost 100-fold higher than the safe intake of 0.0015 mg/child (5 kg) and only about three times lower than the LOAEL seen in animal studies (Pohl and Tylenda, 2000). Establishing the chronic RfD value of USEPA, a safe intake for a child with 5 kg would be even lower (0.0003 mg/kg) and would exceed the RfD 462-fold. Also in other regions intake levels with food and especially with breast milk are of high concern.

Anyway the unique social, cultural, spiritual and economic values of traditional foods have to be considered and strong efforts should be taken to minimize beta-HCH levels therein (CACAR, 2003).

2.4.2   Environment

Beta-HCH is acutely toxic to aquatic organisms. Compared to effect concentrations in algae and daphnia (IPCS, 1992), fish is the most sensitive taxon. An LC50 of approximately 1.7 mg/l was determined in an acute test (duration 24 hours) in zebra fish and neon (Oliveira-Filho and Paumgarten, 1997). IPCS (1992) reported an EC50 based on changes in fish behaviour of 47 µg/l (96 hours) and an LC50 in guppy of 0.9 mg/l (48 hours). In a prolonged toxicity study (duration 4 and 12 weeks) including histopathological changes, the NOEC in young guppy was 32 µg/l (Wester and Canton, 1991). Estrogenic activity of beta-HCH occurred in the form of alterations of vitellogenin production, testis atrophy, hermaphroditism in male and pituitary changes.

It seemed that beta-HCH is not very toxic to birds (IPCS, 1992) but that it may affect reproduction. In female birds with high concentrations of various organochlorines including beta-HCH, the body condition of the first and second chicken in the clutch was poorer (AMAP, 2004).

Monitoring data on effects in Svalbard polar bears revealed a significant negative correlation between retinol and HCHs (AMAP, 2004). Retinol is essential as it is required in reproduction, embryonic and foetal development, as well as in vision, growth, differentiation and tissue maintenance.

3   Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 5-14 % beta-HCH and was used extensively worldwide as organochlorine pesticide.

Though usage of technical HCH is currently negligible, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles, landfills, or dumping grounds. Though no quantitative estimates of these releases exist, the amounts of HCH-residuals in the form of by-products from lindane production were estimated to range between 1.6-1.9 to 4.8 million tonnes. In addition many of local sources are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of beta-HCH allow on a global scale for "cold condensation", but pathways of alpha- and beta-HCH diverge in the environment. Reasons are possibly greater physical and metabolic stability, higher water/octanol solubility, a lower Henry's Law Constant and a relatively high octanol-air partition coefficient, which favours partitioning to organic phases.

According to available data beta-HCH can be considered to be persistent in the environment. Though beta-HCH is biodegradable by various microbial strains under favourable conditions degradation rates in field experiments are low indicating very slow decrease under environmental conditions. Residues of beta-HCH remained for years in treated plots in several studies. The only determined DT50 values were 100 and 184 days on cropped and uncropped soil under subtropical conditions. In addition to degradation and plant up-take volatilisation and leaching may also have contributed to the disappearance of beta-HCH in this investigation.

Monitoring data from remote regions far from sources clearly indicate that beta-HCH has undergone long-range environmental transport. It is suggested that beta-HCH enters the Arctic by ocean currents passing through the Bering Strait after wet deposition and partitioning into the North Pacific Ocean.

Beta-HCH has a BCF (whole body) of 1 460 based on a laboratory study in fish. However, there are several field investigations in Arctic marine food webs available that suggest that beta-HCH may accumulate to high concentrations in upper trophic levels (i.e. marine mammals and birds). Thus BMFs as well as FWMFs were greater than 1. It has further been demonstrated that beta-HCH is found in breast milk of highly exposed indigenous mothers who consume a subsistence diet. Thus its high bioaccumulation potential is well documented.

Beta-HCH has been shown to be neurotoxic, hepatotoxic, to cause reproductive and immunosuppressive effects and effects on fertility and reproduction in laboratory animals.

Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions.

The International Agency for Research on Cancer (IARC) has classified beta-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer, at least beta-HCH is a known tumour promoting agent. Beta-HCH may adversely affect human health in contaminated areas and as well in Arctic regions. Based on the available toxicity data of beta-HCH it can be concluded that current concentrations of beta-HCH in food and human milk in these regions are of concern. The estimated cancer risk calculated by EPA, though very conservative, seems very high (5.0×10^{-3} to 7.7×10^{-4}).

It has to be taken into consideration that the Arctic population and wildlife are also exposed against a wide range of other persistent toxic substances, which may act in an additive way. Nevertheless it should be emphasized that traditional foods have unique social, cultural, spiritual and economic value and therefore it is strongly recommended to avoid foods in which beta-HCH levels are of concern.

4   Concluding statement

Though most countries have banned or restricted the use of technical HCH as a pesticide, replacing it in most cases by the use of lindane, the production process creates huge amounts of HCHs residuals. The continued production and existing stockpiles of these waste isomers have been a worldwide problem and contribute to the releases into the environment.

Beta-HCH is persistent and present in all environmental compartments; especially levels in the terrestrial as well as in the aquatic food chain give rise to concern to adversely affect human health. High exposure is expected in polluted areas, which are still present around the globe. High exposure ois also possibly expected as a result of long-range environmental transport.

Based on the inherent properties, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006

Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on lindane

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on lindane, on the basis of the draft contained in document UNEP/POPS/POPRC.2/10. The text of the risk profile, as amended, is provided below. It has not been formally edited.

LINDANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

CONTENTS

Executive summary

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention. The Review Committee evaluated Annex D information presented by Mexico at its first meeting and concluded that "Lindane meets the screening criteria specified in Annex D".

International initiatives on Lindane include the Protocol on Persistent Organic Pollutants of the Convention on Long Range Transboundary Air Pollution; the Rotterdam Convention; the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic, the Great Lakes Binational Toxics Strategy between the United States and Canada, and a North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane Isomers under the Commission for Environmental Cooperation between Canada, United States and Mexico.

For each ton of lindane produced, around 6-10 tons of other isomers are also obtained. In the last years the production of lindane has rapidly decreased and it appears that only Romania and India are current producing countries. Lindane has been used as a broad-spectrum insecticide for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications.

Once released into the environment, lindane can partition into all environmental media. Hydrolysis and photolysis are not considered important degradation pathways and reported half-lifes in air, water and soil are: 2.3 days, 3-300 days and up to 2 to 3 years, respectively. A half-life of 96 days in air has also been estimated.

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. The bioconcentration factors in aquatic organisms under laboratory conditions ranged from approximately 10 up to 4220 under field conditions, the bioconcentration factors ranged from 10 up to 2600. Although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are also relatively rapid, once exposure is eliminated.

Many studies have reported lindane residues throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine contaminants in the Arctic where they have not been used, pointing at evidence of their long-range transport.

The hypothesis that isomerization of gamma HCH to alpha HCH in air emerged as a possible explanation for higher than expected alpha HCH/gamma HCH ratios in the Arctic. However no conclusive experimental evidence of isomerization taking place in air has been produced to date. Also, although there is evidence that bioisomerization of lindane can take place through biological degradation, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH.

Lindane can be found in all environmental compartments, and levels in air, water, soil sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk in different studies in diverse countries. Exposure of children and pregnant women to lindane are of particular concern.

Hepatotoxic, immunotoxic, reproductive and developmental effects have been reported for lindane in laboratory animals. The US EPA has classified lindane in the category of "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds, and decreased body weight gain in mammals, with some effects indicative of endocrine disruption.

These findings and the evidence of its long range transport, as well as the fact that lindane is currently the object of local and global action initiatives, that also include thorough analysis and selection procedures, should be sufficient to warrant global action under the Stockholm Convention.

1. Introduction

1.1 Chemical identity

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention on June 29, 2005. The proposal presented data on the gamma isomer, but mentioned as well that "other isomers of hexachlorocyclohexane should also be considered in this proposal".[1]

Lindane: gamma-hexachlorocyclohexane
Chemical formula: $C_6H_6Cl_6$
CAS number: 58-89-9
Molecular weight: 290.83

Physical and Chemical properties of gamma-HCH

Physical state	Crystalline solid
Melting point	112.5 °C
Boiling point at 760 mmHg	323.4 °C
Vapor pressure at 20°C	4.2×10^{-5} mmHg
Henry's Law constant at 25°C	3.5×10^{-6} atm m^3/mol

ATSDR, 2005

Lindane is the common name for the gamma isomer of 1,2,3,4,5,6-hexachlorocyclohexane (HCH). Technical HCH is an isomeric mixture that contains mainly five forms differing only by the chlorine atoms orientation (axial or equatorial positions) around the cyclohexane ring. The five principal isomers are present in the mixture in the following proportions: alpha-hexachlorocyclohexane (53%–70%) in two enantiomeric forms ((+)alpha-HCH and (-)alpha-HCH), beta-hexachlorocyclohexane (3%–14%), gamma-hexachlorocyclohexane (11%–18%), delta-hexachlorocyclohexane (6%–10%) and epsilon-hexachlorocyclohexane (3%–5%). The gamma isomer is the only isomer showing strong insecticidal properties.

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[1] UNEP/POPS/POPRC.1/8 and UNEP/POPS/POPRC.1/INF/8

Structure of alpha, beta, gamma, delta and epsilon HCH isomers
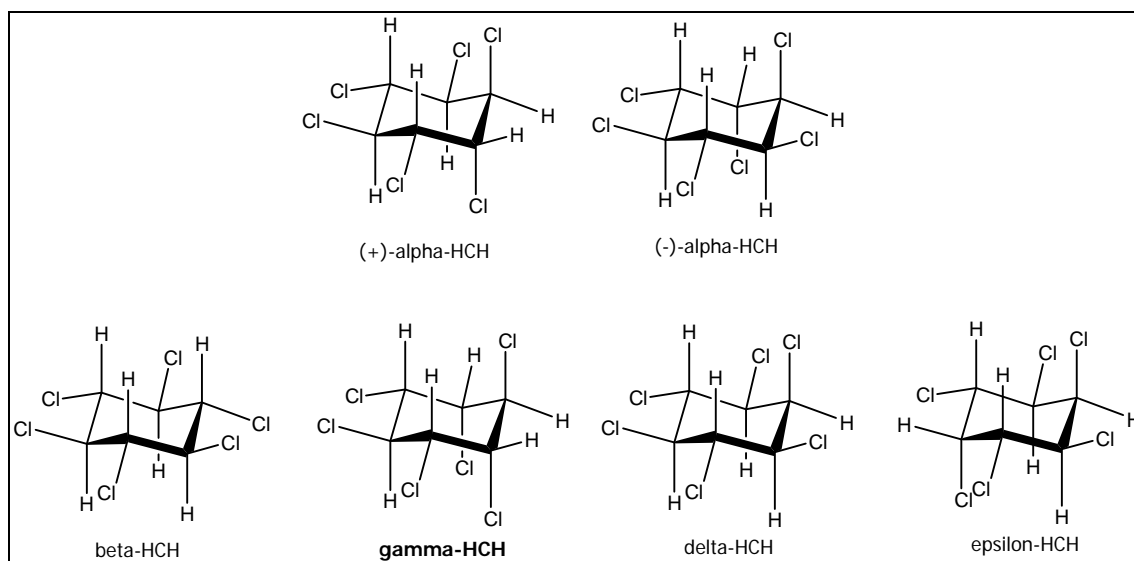
Modified from Buser et al., 1995.

The term "benzene hexachloride (BHC)" is also commonly used for HCH, but according to IUPAC rules this designation is incorrect. Nevertheless the term is used and therefore, gamma-BHC also designates lindane. In the present risk profile document, lindane refers to at least 99% pure gamma-HCH and the BHC term is not used.

1.2   Conclusion of the Review Committee regarding Annex D information

The Committee has evaluated Annex D information at its first meeting held in Geneva, from November 7th to 11th 2005, and has decided that "the screening criteria have been fulfilled for lindane" and concluded that "Lindane meets the screening criteria specified in Annex D." The Committee agreed that the alpha and beta isomers could be included in the discussions, although any decision to propose inclusion of the chemical in the Convention would apply only to lindane, the gamma isomer[2].

1.3   Data sources

Data sources provided by the proposing party, Mexico:
1. ATSDR Toxicological Profile Information Sheet 2001
2. AMAP. 1998. Persistent Organic Pollutants. Arctic Monitoring and Assessment Program (AMAP), 183-373. Oslo, Norway.
3. DeVoto, E., L. 1998. *Arch. Environ. Health* 53:147-55.
4. Extoxnet.1996. USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.
5. Gregor, 1989. Environ. Sci. technol. 23: 561-565.
6. IARC Monographs, http://monographs.iarc.fr
7. Mössner, S., 1994. Fres. J. Anal Chem. 349: 708-16.
8. Raum, E, A. 1998. *J. Epdiem. Commun. Health* 52 (suppl 1): 50S-5S.

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[2] UNEP/POPS/POPRC.1/10

9. U.S Environmental Protection Agency. IRIS.
10. Walker, K., 1999. Environ. Sci. Technol. 33:4373-4378.
11. Wania,F., 1999. Environ. Toxicol. Chem. 18: 1400-1407.
12. WHO. 1991. Environmental Health Criteria 124 Lindane
13. Willett, K., 1998. Environ. Sci. Technol. 32: 2197-207.
14. Yi, F. L., Sci. and Technol. Vol 30, No 12, 1996.

Data sources used by the Committee:
1. UNEP/POPS/POPRC.1/8
2. Nagabe, et al., *Environmental Science and Technology.* 27: 1930–1933. 1993.
3. Harner, T. et al., *Environmental Science and Technology.* 33: 1157–1164. 1999.
4. Harner, T. et al., *Geophysical Research Letters.* 27: 1155–1158. 2000.
5. *Environmental Health Criteria No. 124*: *Lindane*. International Programme on Chemical Safety.
6. UNEP, ILO, WHO. Geneva. 1991. (http://www.inchem.org/documents/ehc/ehc/ehc124.htm).
7. Brock et al., *Alterra Report* 89, Netherlands. 2000.
8. *Guidance document on risk assessment for birds and mammals under Council Directive*
9. *91/414/EEC*. European Union. SANCO/4145/2000 – final, Brussels. 2002.
10. Arctic Monitoring and Assessment Programme. Norway. 2002.
11. Gregor, D., et al., *Environmental Science and Technology.* 23: 561–565, 1989.
12. Brubaker, W. W., and Hites, R.A. 1998. *Environmental Science and Technology* 32: 766–769.

The following parties and observers have answered the request for information specified in Annex E of the Convention: Republic of Macedonia, International HCH & Pesticides Association, Republic of Armenia, Haiti, World Wild Fund for Nature, CropLife International, International POPs Elimination Network, Morocco, Republic of Mauritius, European Community, Brazil, Republic of Lithuania, Canada, United States of America, Australia, Japan, Mexico, Lebanon and Poland. A more elaborated summary of the submissions is provided as separate **UNEP/POPS/POPRC.2/INF.18** document. *Summary of data submitted by Parties and observers for information specified in Annex E of the Convention*.

The following lindane assessment reports are publicly available through the internet:

- Assessment of Lindane and other Hexachlorocyclohexane Isomers. USEPA. February 2006 http://www.epa.gov/fedrgstr/EPA-PEST/2006/February/Day-08/p1103.htm

- Toxicological Profile for Hexachlorocyclohexane, Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, updated in 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- USEPA Reregistration Eligibility Decision (RED) for Lindane. 2002. See RED and supporting health and eco assessments included in the docket. http://www.epa.gov/oppsrrd1/REDs/lindane_red.pdf

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for Public Comment. October 2005. North

American Commission for Environmental Cooperation http://www.cec.org/files/PDF/POLLUTANTS/Lindane-NARAP-Public-Comment_en.pdf

- Health risks of persistent organic pollutants from long-range transboundary air pollution, Joint WHO/convention task force on the health aspects of air pollution. WHO/Europe. 2003. Chapter 3: Chapter 3/ Hexachlorocyclohexanes http://www.euro.who.int/Document/e78963.pdf

- Technical Review Report on Lindane. Reports on Substances Scheduled for Re-assessments Under the UNECE POPs Protocol. Prepared by Austria in 2004 (available: http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf)

- IPCS International Programme on Chemical Safety. Health and Safety Guide No. 54 LINDANE (Gamma-HCH) HEALTH AND SAFETY GUIDE. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva, 1991. http://www.inchem.org/documents/hsg/hsg/hsg054.htm

1.4   Status of the chemical under international conventions

Lindane is listed as a "substance scheduled for restrictions on use" in Annex II of the 1998 **Protocol on Persistent Organic Pollutants of the Convention on Long-Range Transboundary Air Pollution**. This means that products in which at least 99% of the HCH isomer is in the gamma form (i.e. lindane, CAS: 58-89-9) are restricted to the following uses: 1. Seed treatment. 2. Soil applications directly followed by incorporation into the topsoil surface layer 3. Professional remedial and industrial treatment of lumber, timber and logs. 4. Public health and veterinary topical insecticide. 5. Non-aerial application to tree seedlings, small-scale lawn use, and indoor and outdoor use for nursery stock and ornamentals. 6. Indoor industrial and residential applications. All restricted uses of lindane shall be reassessed under the Protocol no later than two years after the date of entry into force. The Protocol entered into force on October 23th, 2003. [3]

Lindane, as well as the mixture of HCH isomers, is listed in Annex III of the **Rotterdam Convention** on the Prior Informed Consent Procedure as "chemicals subject to the prior informed consent procedure". The Rotterdam Convention entered into force 24 February 2004. [4]

Hexachlorocyclohexane isomers, including Lindane, the gamma isomer, are included in the List of Chemicals for Priority Action (Updated 2005) under the **OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic**. Under this initiative, the Hazardous Substance Strategy sets the objective of preventing pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances, with the ultimate aim of achieving concentrations in the marine environment near background values for naturally occurring substances and close to zero for man-made synthetic substances. The OSPAR Convention entered into force on 25 March 1998. [5]

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[3] Convention on Long-range Transboundary Air Pollution   http://www.unece.org/env/lrtap/
[4] Rotterdam Convention http://www.pic.int.
[5] OSPAR Convention for the Protection of the Marine Environment of the Northeast Atlantic. http://www.ospar.org/

HCH (including lindane) is listed as a Level II substance in the **Great Lakes Binational Toxics Strategy** between the United States and Canada, which means that one of the two countries has grounds to indicate its persistence in the environment, potential for bioaccumulation and toxicity. [6]

A North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers is under development under the Sound Management of Chemicals project, which is an ongoing initiative to reduce the risks of toxic substances to human health and the environment in North America. This program is part of the Pollutants and Health Program of the **Commission for Environmental Cooperation** between the three NAFTA countries: Canada, United States and Mexico. (CEC, 2005)

Lindane is also listed under the **European Waterframework Directive**. This Directive is a piece of water legislation from the European Community. It requires all inland and coastal water bodies to reach at least "good status" by 2015. Lindane is one of the listed priority hazardous substances for which quality standards and emission controls will be set at EU level to end all emissions within 20 years. [7]

2.   Summary information relevant to the risk profile

2.1   Sources

a)   Production, trade, stockpiles

The manufacture of technical-HCH involves the photochlorination of benzene, which yields a mixture of five main isomers. This mixture of isomers is subject to fractional crystallization and concentration to produce 99% pure lindane, with only a 10-15 percent yield. The production of lindane is therefore inefficient as for each ton of lindane (gamma isomer) obtained, approximately 6-10 tons of other isomers are also obtained (IHPA, 2006). According to the *International HCH & Pesticide Association* (IHPA) (report and Annexes), there have been variations in the production methods for HCH and lindane, as well as for HCH isomers destruction or re-use. However, most of the methods to process or re-use the waste HCH isomers have been given up over the years and consequently, most of the waste products have been dumped over the last 50 years (IHPA, 2006). The lindane industry claims that modern production technology processes the waste isomers into TCB (trichlorobenzene) and HCl (hydrochloric acid) thereby reducing or eliminating environmental contamination from these byproducts (Crop Life, 2006).

Historical production of technical HCH and lindane occurred in many European countries, including the Czech Republic, Spain, France, Germany, United Kingdom, Italy, Romania, Bulgaria, Poland, and Turkey, and took place mainly from 1950 or earlier and stopped in 1970 to the 1990s . According to a research by IHPA, technical HCH and lindane have also been produced in other countries including Albania, Argentina, Austria, Azerbaijan, Brazil, China, Ghana, Hungary, India, Japan, Russia, Slovakia and the United States. Exact information is difficult to obtain, as many countries do not keep records of historical pesticides production, sales and usage or the industry considers this to be proprietary information (IHPA, 2006).

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[6]   Great Lakes Binational Toxics Strategy http://www.epa.gov/glnpo/gls/index.html
[7]   European Union Water Framework Directive http://ec.europa.eu/environment/water/water-framework/index_en.html

It is estimated that global lindane usage from 1950 to 2000 for agricultural, livestock, forestry, human health and other purposes amounts to around 600 000 tons. The next table shows agricultural lindane usage in different continents in the period from 1950 to 2000 (IHPA, 2006).

Continent	Usage (tons)
Europe	287,160
Asia	73,200
America	63,570
Africa	28,540
Oceania	1,032
Total	**435,500**

It appears that in the last years the production of lindane has rapidly decreased leaving only a small number of producing countries. Romania, India, and possibly Russia are the only countries in the world still currently producing Lindane (IHPA, 2006 and USEPA, 2006, CEC, 2005 Annex A). Other sources indicate that Russia (Li et al., 2004) and China (USEPA, 2006) have stopped producing lindane. India produces and uses lindane for the control of mites in sugarcane at 200 tonnes per year.

Global lindane production between 1990 and 1995 was around 3 222 tons per year. In Europe, the top 10 countries with highest lindane usage between 1950 and 2000, representing 96% of the total usage in Europe, were: Czechoslovakia, Germany, Italy, France, Hungary, Spain, Russia, Ukraine, Yugoslavia and Greece (IHPA, 2006).

The 1998 Food and Agriculture Organization Inventory of Obsolete, Unwanted and/or Banned Pesticides found a total of 2785 tons of technical-grade HCH, 304 tons of lindane, and 45 tons of unspecified HCH material scattered in dumpsites in Africa and the Near East (Walker et al., 1999).

According to the information from the Arctic Council's Arctic Contaminants Action Program (ACAP) project on obsolete pesticides, possibly up to 1,000 tonnes of obsolete stockpiles of technical HCH and lindane still exist in the Russian Federation after the ban of production in the beginning of the 1990s.

b)   Uses

Lindane has been used as a broad-spectrum insecticide, which acts by contact, for both agricultural and non-agricultural purposes. Lindane has been used for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications (WHO, 1991).

As a consequence of its toxic, suspected carcinogenic, persistent, bioaccumulative and suspected endocrine disrupting properties, lindane became a substance of scrutiny for countries in the European Community. All uses of HCH including lindane have been banned, but Member States may allow technical HCH for use as an intermediate in chemical manufacturing and in products with at least 99% of the isomer content in the gamma form (lindane) for public health and veterinary topical use only, until December 31st 2007 (UNECE, 2004). Currently, the only registered agricultural use for lindane in the United States is for seed treatment and for lice and scabies treatment on humans (CEC, 2005). In Canada the major use of lindane has been on canola

and corn, but the only current allowable use of lindane is for public health purposes, as a lice and scabies treatment (CEC, 2005).

Information on current uses as informed by countries may be found on POPRC/LINDANE/INF.1

c)   Releases to the environment

Considering every ton of lindane produced generates approximately 6 - 10 tons of other HCH isomers, a considerable amount of residues was generated during the manufacture of this insecticide. For decades, the waste isomers were generally disposed of in open landfills like fields and other disposal sites near the HCH manufacturing facilities. After disposal, degradation, volatilization, and run off of the waste isomers occurred (USEPA, 2006).

If the estimate of global usage of lindane of 600,000 tons between 1950 and 2000 is accurate, the total amount of possible residuals (if it is assumed that a mean value of 8 tons of waste isomers are obtained per ton of lindane produced) amounts to possibly 4.8 million tons of HCH residuals that could be present worldwide giving an idea of the extent of the environmental contamination problem (IHPA, 2006).

Air releases of lindane can occur during the agricultural use or aerial application of this insecticide, as well as during manufacture or disposal. Also, lindane can be released to air through volatilization after application (Shen et al., 2004). Evaporative loss to air from water is not considered significant due to lindane's relatively high water solubility (WHO/Europe, 2003).

2.2   Environmental fate

Persistence

A half-life for lindane in air of 2.3 days was estimated, based on the rate constant for the vapor-phase reaction with hydroxyl radicals in air; a tropospheric lifetime of 7 days due to gas-phase reaction with hydroxyl radicals was estimated, and a lifetime of 13 days was estimated for atmospheric reaction with OH radicals in the tropics (Mackay, 1997). Brubaker and Hites (1998) estimated a lifetime in air of 96 days for lindane. Lindane has half-lifes of 3-30 days in rivers and 30 to 300 days in lakes. Other studies report calculated or experimental hydrolysis half-lifes ranging from 92 to 3090 hours depending on the study; a persistence of about 2 to 3 years in soil is also reported (Mackay et al., 1997).

Once released into the environment, lindane can partition into all environmental media, but it is demonstrated that evaporation is the most important process in the distribution of lindane in the environment. Several studies focusing on the adsorption-desorption characteristics of lindane have shown that mobility of lindane is very low in soils with a high content of organic material, and higher in soils with little organic matter. The diffusion of lindane has also been investigated, showing it is strongly influenced by the water content of the soil and by temperature. The International Program on Chemical Safety states that when lindane suffers environmental degradation under field conditions, its half-life varies from a few days to three years depending on many factors including climate, type of soil, temperature and humidity (WHO, 1991).

Hydrolysis is not considered an important degradation process for lindane in aquatic environments under neutral pH conditions. Lindane is stable to hydrolysis at pH 5 and 7 with a half-life of 732 days and a half-life of 43 to 182 days at pH 9. Also, different estimated and calculated half-life values for lindane have been reported to be: 1.1 years at pH 8 and 20°C in seawater; 42 years at pH 7.6 and 5°C in Lake Huron, and 110 years in the Arctic Ocean at pH 8 and 0°C (USEPA, 2006).

Lindane is stable to light. Since lindane does not contain chromophores that absorb light, direct photolysis either in air, water or soil is not expected to occur. Even when indirect photolysis could occur with a photosensitizing agent, there is no clear evidence of lindane photodegradation. Lindane degrades very slowly by microbial action with a calculated half-life in soil of 980 days under laboratory aerobic conditions. Degradation takes place faster under anaerobic conditions than in the presence of oxygen. Possible degradation products are pentachlorocyclohexene, 1,2,4,-trichlorobenzene, and 1,2,3-trichlorobenzene (USEPA, 2006).

Bioaccumulation

The bioconcentration factors (BCF) in aquatic organisms under laboratory conditions ranged from approximately 10 up to 6000; under field conditions, the bioconcentration factors ranged from 10 up to 2600 (WHO, 1991). Other studies report bioconcentration factors (log BCF) ranging from 2.26 in shrimp to 3.85 in rainbow trout in early life stages on lipid basis and 4.3 in zooplankton and a bioaccumulation factor (log BAF) up to 4.1 in rainbow trout (Mackay et al., 1997). Also, uptake and elimination rate constants ranging from $180 - 939$ h^{-1} and $0.031 - 0.13$ h^{-1} respectively have been reported for rainbow trout in early life stages on lipid basis (Mackay et al., 1997).

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. Bioconcentration factors (BCF) within aquatic species vary considerably, with experimental data revealing bioconcentration factors of 3-36 (Berny, 2002); 43-4220 on a wet weight basis, and a mean BCF of 11,000 on a lipid basis (Geyer et al., 1997); and also 1200-2100 (Oliver et al., 1985).

An average log BCF of 2.28 in invertebrate species and an average log BCF of 2.87 in vertebrate species can be calculated from different studies (Donkin et al., 1997, Renberg et al., 1985, Thybaud et al., 1988, Yamamoto et al., 1983, Butte et al., 1991, Carlberg et al., 1986, Kanazawa et al., 1981, Kosian et al., 1981 La Rocca et al., 1991, Oliver et al., 1985, Vigano et al., 1992). In the same way, an average log BAF of 2.94 in invertebrate species, and an average log BAF of 3.80 in vertebrate species can be calculated from other studies (Oliver et al., 1988, Chevreuil et al., 1991, Hartley et al., 1983, Caquet et al., 1992). Bioconcentration factors of 780 for fillet, 2500 for viscera and 1400 for whole fish tissues have also been reported (USEPA, 2002).

In an experiment carried out by Geyer et al. (1997), bioconcentration factors are shown to be dependent on the fish species and their lipid content; additionally, different modes of uptake, metabolism, sources of contamination and even experimental conditions, taken together could explain the significant variation observed for BCF values. Also, most data suggest that, although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are relatively rapid once exposure is eliminated. (WHO, 1991).

The bioaccumulation of lindane has been observed for most taxonomic groups, from plants and algae to vertebrates. The environmental consequences of the combination of this bioaccumulation potential with a high toxicity – no-observed-adverse-effect levels (NOAELs) as low as 0.3 mg/kg body weight/day – and ecotoxicity – aquatic ecosystem no-observable-effect concentration (NOEC) below 1 μg/l (*Environmental Health Criteria No. 124, 1991;* and Brock et al., 2000) – should be

considered. For example, when measured field levels in earthworms (0.3 mg/kg for a soil containing 80 µg/kg) are weighed against mammalian toxicity data (*Environmental Health Criteria No. 124, 1991;*) using a realistic food intake ratio of 0.63 (*Guidance document on risk assessment for birds and mammals* 2002.) the comparison indicates an area of ecotoxicological concern which should be further explored.

Lindane has been reported in seabirds, fish and mammals in the Arctic (ATSDR, 2005). Lindane concentrations in marine mammals are found at equivalent or even higher levels than some of the more hydrophobic contaminants such as polychlorinated biphenyls (PCBs) and DDT (ATSDR, 2005). In addition, lindane has been reported in human breast milk among Inuit in the Arctic and in marine mammals (Arctic Monitoring and Assessment Programme, 2002).

Potential for long-range environmental transport

Many studies have reported HCH residues, particularly alpha and gamma isomers throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine insecticide contaminants in the Arctic, and their presence in the Arctic and Antarctic, where technical HCH and lindane have not been used, is evidence of their long-range transport. HCH isomers, including lindane, are subject to "global distillation" in which warm climates at lower latitudes favor evaporation into the atmosphere where the chemicals can be carried to higher latitudes. At midlatitudes, deposition and evaporation vary with season. At high latitudes, cold temperatures favor deposition (Walker et al., 1999).

Use of lindane in countries such as Canada, where usage was ~ 500 tons in 2000, and certain European countries, such as France, has contributed to gamma-HCH levels present in the Arctic air. Concentrations of lindane were detected at Alert in the Arctic and varied from 10-11 pg/m^3 in 1993 decreasing to 6.4 pg/m^3 in 1997 (CACAR, 2003).

In a study completed by Shen et al. in 2004, 40 passive air sampling stations were located along transects from the Canadian Arctic, down the east coasts of Canada and the U.S., along the Canada - U.S. border and in southern Mexico and Central America for one year. The elevated alpha-HCH levels (sampler volumetric air concentrations between 1.5 and 170 pg/m^3) in eastern Canada were explained by outgassing of alpha-HCH from cold arctic water flowing south, warming, and releasing the alpha-HCH back to the atmosphere. High concentrations of gamma-HCH (sampler volumetric air concentrations between 5 and 400 pg/m^3) were found in the Canadian prairies, north of Lake Ontario, southern Québec, the middle Atlantic states and southern Mexico, reflecting the influence of regional lindane usage (Shen et al., 2004). Transport over the Pacific Ocean of lindane was measured at a sampling site in Yukon and ranged 4-18 pg/m^3 (Bailey et al., 2000). HCH isomers, including lindane, were measured at a mountain site at Tenerife Island from June 1999 to July 2000. Air concentrations of gamma-HCH at this site ranged 18 - 31 (mean 26) pg/m^3 (Van Drooge et al., 2002).

Lindane is very prevalent in the marine environment and soils, and its atmospheric long range transport potential has been demonstrated for the European Union, (WHO/Europe, 2003) especially by the European Monitoring and Evaluation Program (EMEP). High concentrations of gamma-HCH in air occurred in France, Portugal, Spain, the Netherlands and Belgium. These can be explained by the high emission densities of lindane in these countries. Relatively high air concentrations were also found in Germany, Italy, Switzerland and Luxembourg, despite the lower

lindane emission densities in these countries. These elevated air concentrations were probably explained by atmospheric transport from the former high-density emission European countries (Shatalov and Malanichev, 2000; Shatalov et al., 2000).

a)   Isomerization

The hypothesis that isomerization of gamma-HCH to alpha-HCH could be taking place in air emerged as a possible explanation for alpha-HCH/ gamma-HCH ratios that were found in the 80's as high as 18, when this ratio was expected to be around 5 according to the fraction of these two isomers found in the technical HCH mixture. (Oehme et al 1984a, Oehme et al., 1984b, Pacyna et al., 1988) However no conclusive experimental evidence of isomerization taking place in air has been produced to date.

In the same line, Walker et al. (1999) noted that if photochemical transformation of gamma-HCH to alpha-HCH in air takes place, one should see significant concentrations of alpha-HCH in the Southern Hemisphere air. However, recent measurements have found alpha-HCH levels are dropping over time in the Southern Hemisphere as well as in the Arctic Ocean, which is not consistent with the isomerization theory and a continued use of lindane. The ratio of alpha-HCH/gamma-HCH in air sampled in the Southern Hemisphere during the 1980s - 1990s was generally 1 to 2.3 (Ballschmiter et al., 1991, Bidleman et al., 1993, Iwata et al., 1993, Kallenborn et al., 1998, Lakaschus et al., 2002; Schreitmüller et al., 1995) and was 0.81 in the most recent study in Antarctica (Dickhut et al., 2005).

Other studies have suggested that differential air-sea gas exchange rates could lead to fractionation of the HCH isomers and preferential accumulation of alpha-HCH in air during long range transport over the oceans. This could account for some portion of the elevated alpha-HCH/gamma-HCH ratios observed during wintertime, but not for the very high ratios found in summer in the early studies. (Pacyna et al., 1988 and Oehme et al., 1991). Walker et al. (1999) concluded that even when the experiments show that photoisomerization is possible, evidence that this process is a substantial contributor to the high alpha/gamma ratios observed in the Arctic is indirect and subject to several interpretations.

Several studies have also reported photolytic isomerization of gamma-HCH to alpha-HCH. However, these studies have demonstrated isomerization in condensed media, but there is no evidence that isomerization takes place in the gas phase under ambient atmospheric conditions. Laboratory evidence shows that gamma-HCH can be transformed into other isomers in soil or sediments through biological degradation, but although the bioisomerization of lindane can take place, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH (Walker et al., 1999 and Shen et al., 2004).

b)   Environmental monitoring data

Poland reported concentrations of gamma-HCH in river sediments ranging from 2.4 to 9.4 µg/kg. Results from the National Veterinary Residue Control Programme in Poland indicate that food of animal origin contains levels of gamma-HCH below the level of action of 1000 µg/kg (Annex E information provided by Poland, 2006).

The Ministry of Environment in Japan has monitored Lindane in water finding a concentration of Lindane of 32 to 370 pg/l in 60 surveyed water specimens across the country in 2003. A total of 186 bottom sediment specimens were also surveyed in 2003 and Lindane was detected in all the

specimens, with a concentration of Lindane from traces (1.4) to 4000 pg/g dry, with a geometric mean of 45 pg/g dry. A recent survey in 2003 on shellfish, fish and birds shows that Lindane was detected in all the specimens with concentrations ranging from 5.2 to 130 pg/g-wet for shellfish, 130 pg/g-wet for fish, and 1,800 to 5,900 pg/g-wet for birds. Lindane was detected in all 35 specimens from 35 sites in Japan for ambient air in the warm season in 2003 with a concentration of Lindane ranging from 8.8 to 2,200 pg/m^3 with a geometric mean of 63pg/m^3. The survey on the same sites excluding one site during the cold season in year 2003 indicates a concentration of 3.1 to 330 pg/m^3 with a geometric mean of 14pg/m^3 (Annex E information provided by Japan, 2006).

Australia reported that none of the meat and crop samples monitored for residues in the country contained detectable levels of lindane (Annex E information provided by Australia, 2006).

The United States reported that gamma-HCH, was below the level of detection in all samples analyzed for the Third National Report on Human Exposure to Environmental Chemicals. Lindane was detected in fish tissue from lakes and reservoirs in the US EPA national Lake Fish Tissue Study, with levels ranging from 0.652 to 8.56 ppb. Lindane is being monitored in air and precipitation with the Integrated Atmospheric Deposition Network in the Great Lakes region with average concentration of 15-90 pg/m^3 in the early 90s, decreasing to 5-30 pg/m^3 since 2000. Average concentrations in precipitation (volume-weighted mean) at seven main sites during the years 1997- 2003 were 690-1400 pg/L for lindane. The most recent years of available analytical data in the U.S. EPA's Great Lakes Fish Monitoring Program indicate the concentration of Lindane in sport fish fillets (Chinook and Coho Salmon and Steelhead Trout) have ranged between trace detection and 0.005 ppm between 1982 and 2000. The National Oceanic and Atmospheric Administration's National Status and Trends (NS&T) Program has measured lindane in the tissues of bivalves throughout the coastal US and Great Lakes from 1986 to present. Over the Program's history, a total of 283 sites throughout the contiguous US, Alaska, Hawaii, and Puerto Rico have been sampled, with a total of 4,990 records for the gamma isomer. Median measured concentration for gamma-HCH was 0.56 (range 0-71.0) ng/g dry weight. A trends assessment using data pooled for the entire USA, indicates that there has been a statistically significant decline in lindane levels from 1986 through 2003. (Annex E information provided by the United States of America, 2006).

In Canada, a project was undertaken in 1999-2000 by Alberta Environment to characterize the pesticides found in a number of Alberta locations, and to determine their relative levels and seasonality. Lindane was detected in ambient air at Lethbridge in all samples starting from May to August. Lindane levels peaked on June 15 at 1.15 ng/m^3, while the low level of 0.23 ng/m^3 was present in ambient air on June 22, 1999. As lindane is used on treated seed that is planted in April and early May, lindane is then released into the atmosphere following seeding and hence the higher levels in May followed by a slow decline to low and/or undetectable levels in August and September (Kumar, 2001).

2.3   Exposure

Lindane can be found in all environmental compartments and levels in air, water, soil, sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk (WHO/Europe, 2003).

A special area of concern is the fact that HCH isomers, including lindane, accumulate in colder climates of the world. High concentrations of HCH isomers, including lindane, are found in the

Beaufort Sea and Canadian Archipelago (CEC, 2005). Through environmental exposure, gamma-HCH can enter the food chain and accumulate in fatty animal tissue constituting an important exposure pathway for Arctic or Antarctic animals as well as for humans who rely on these animals for their subsistence diets (USEPA, 2006)

General population exposure to gamma-HCH can result from food intake, particularly from animal origin products like milk and meat, as well as water containing the pesticide. Lindane was found to be 10 times higher in adipose tissue of cattle than in the feed (ATSDR, 2005) showing that animals may be exposed to the compound through food and even through ectoparasite treatment. Lindane has been detected in cow's milk in countries that still use the chemical as a pesticide. In a study performed in Uganda, Africa, the concentrations of gamma-HCH in cow's milk was 0.006–0.036 mg/kg milk fat, respectively. Mean levels of gamma-HCH analyzed in cow's milk samples from two separate areas in India were 0.002 and 0.015 mg/kg. A monitoring study of 192 samples of cow's milk from Mexico revealed 0.002–0.187 mg/kg of gamma-HCH (ATSDR, 2005).

Determinations of the lindane content in body tissues in the general population have been made in a number of countries. The content in blood in the Netherlands was in the order of < 0.1–0.2 μg/l. In the early 1980s, mean concentrations of gamma-HCH in human adipose tissue in Czechoslovakia, the Federal Republic of Germany and the Netherlands were 0.086, 0.024–0.061 and 0.01–0.02 mg/kg, respectively, on a fat basis. In total-diet and market-basket studies to estimate daily human intake of gamma-HCH, clear differences were observed with time: intake in the period around 1970 was up to 0.05 μg/kg body weight per day, whereas by 1980 intake had decreased to 0.003 μg/kg body weight per day or lower (WHO/Europe, 2003).

Individuals living in rural areas and on a non-vegetarian diet are more likely to be exposed to gamma-HCH as shown by a study performed in India, where women who consumed red meat, eggs and chicken had higher pesticide levels, including lindane, in blood than vegetarian women (ATSDR, 2005). Other sources of direct exposure include facilities at which lindane is still being produced, abandoned pesticide plants, and hazardous waste sites (USEPA, 2006).

Exposure of children to lindane is a particular concern. Gamma-HCH has been found in human maternal adipose tissue, maternal blood, umbilical cord blood and breast milk. Lindane has also been found to pass through the placental barrier. Mean breast milk concentration of lindane was 0.084 mg/l in a study in India. An average level of 6 ppb lindane in breast milk was obtained in a study in Alberta, Canada (ATSDR, 2005). In a study looking at organochlorine pesticides in human breast milk collected from 12 regions in Australia, lindane was detected in all samples with a mean of 0.23 ng/g lipid and a range of 0.08-0.47 ng/g lipid (Annex E information provided by Australia, 2006).

Lindane levels have also been found in human breast milk from different countries including Canada, Germany, the Netherlands and the United Kingdom. Lindane levels ranged from <0.001 to 0.1 mg/kg on a fat basis (WHO/Europe, 2003).

An additional exposure route for children exists in regions where lindane is applied directly to milk and meat producing livestock for pest control. On a body weight basis, children consume more milk per unit body weight than adults, and thus may be exposed to significant concentrations of lindane residues through drinking milk (CEC, 2005). Medical use of products to treat head lice and scabies is also of concern when applied to children, although most adverse effects have been observed after misuse. Another exposure to possibly significant amounts of lindane might occur through household dust in certain conditions, and are also of concern especially for children (ATSDR, 2005).

2.4   Hazard assessment for endpoints of concern

Lindane is the most acutely toxic HCH isomer affecting the central nervous and endocrine systems. In humans, effects from acute exposure at high concentrations to lindane may range from mild skin irritation to dizziness, headaches, diarrhea, nausea, vomiting, and even convulsions and death (CEC, 2005). Respiratory, cardiovascular, hematological, hepatic and endocrine effects have also been reported for humans, following acute or chronic lindane inhalation. Hematological alterations like leukopenia, leukocytosis, granulocytopenia, granulocytosis, eosinophilia, monocytosis, and thrombocytopenia, have been reported, following chronic human occupational exposure to gamma-HCH at production facilities (ATSDR, 2005).

Additionally, gamma-HCH has been detected in the blood serum, adipose tissue and semen of occupationally and environmentally exposed individuals (ATSDR, 2005). Serum luteinizing hormone levels were significantly increased in men occupationally exposed to gamma-HCH. Also, the mean serum concentration of follicle stimulating hormone was increased and testosterone was decreased in exposed individuals, but these trends were not statistically significant compared to unexposed controls (ATSDR, 2005).

The most commonly reported effects associated with oral exposure to gamma-HCH are neurological. Most of the information is from case reports of acute gamma-HCH poisoning. Seizures and convulsions have been observed in individuals who have accidentally or intentionally ingested lindane in insecticide pellets, liquid scabicide or contaminated food (WHO/Europe, 2003).

In India, blood levels of gamma-HCH were significantly higher in 135 breast cancer patients, 41-50 years of age, compared to a control group without the disease. However, in similar studies in other countries, a correlation between breast cancer incidence and elevated levels of gamma-HCH in blood was not observed (ATSDR, 2005).

Rats exposed to various concentrations of gamma-HCH through inhalation for 4 hours exhibited concentration-related neurological effects when observed for up to 22 days after exposure. Slight-to-moderate sedation was observed after exposure to 101 mg/m^3; slight-to severe sedation was noted after exposure to 378 mg/m^3; restlessness, excitation, and ataxia were seen after exposure to 642 and 2,104 mg/m^3; and spasms were also noted at the highest concentration of 2,104 mg/m^3 (ATSDR, 2005).

Hepatotoxic effects of lindane have been demonstrated in laboratory animals by numerous studies. Increases in cytochrome P-450 levels after inhalation of lindane aerosol at 5 mg/m^3 for 90 days and increases in cytochrome P-450 activity cytoplasmic superoxide dismutase, lipid peroxidation in rats after being fed 1.8 mg/kg body weight for 15 and 30 days, have been demonstrated. Chronic studies with a dose of 7-8 mg/kg body weight of lindane in the diet showed liver necrosis and fatty degeneration in rats exposed for 38 to 70 weeks, and hypertophy in Wistar rats exposed for 104 weeks (WHO/Europe, 2003). Rats exposed to 15 mg gamma-HCH/kg/day for 5 days and 2.5 mg gamma-HCH/kg/day for 21 days, showed significant increases in absolute liver weight, P-450 and EROD activity in a dose- and time-dependent manner (ATSDR, 2005).

Some evidence is available for immunotoxic effects, like immunosuppression and suppressed antibodies responses, caused by lindane in laboratory animals. Immunosuppression was observed in rats exposed to 6.25 and 25 mg/kg body weight for 5 weeks. Primary antibody response was

suppressed in albino mice being exposed to 9 mg/kg body weight per day in the diet for 12 weeks, and secondary antibody response suppression was observed after 3 weeks at the same dose (WHO/Europe, 2003).

Reproductive effects of lindane have been recorded in laboratory animals: female rats exposed orally to 10 mg/kg body weight per day for 15 weeks presented anti-estrogenic properties. Female rabbits exposed to gamma-HCH at 0.8 mg/kg body weight per day, 3 days per week for 12 weeks had a reduced ovulation rate (WHO/Europe, 2003). In male rats, reductions in the number of testicular spermatids and epididymal sperms were observed after an oral dose of 6 mg/kg body weight for 5 days, or a single dose of 30 mg/kg body weight of gamma-HCH. Testicular atrophy, seminiferous tubules degeneration and disruption of spermatogenesis were also reported in male rats fed 75 mg/kg body weight per day for 90 days (WHO/Europe, 2003). Lindane has therefore characteristics of an endocrine disrupting compound. Exposure to lindane during gestation with a single dose of 30 mg/kg of body weight at day 15 of pregnancy, induced altered libido and reduced testosterone concentration in male offspring rats (USEPA, 2006).

Developmental effects of lindane have also been reported. Decreased fetal weight, fetal thymic weight, and placental weight were observed in mice treated at 30 and 45 mg/kg by gastric intubation at day 12 of gestation. Fetotoxic effects of lindane were also observed and may be due to induced oxidative stress, enhanced lipid peroxidation and DNA single strand breaks in the fetal and placental tissues (WHO/Europe, 2003). Rats exposed to 1.7, 3.4 and 6.8 µM corresponding to exposure doses that might be encountered in contaminated vegetables (80-250 µg/kg) or contaminated drinking water (0.02 µg/l) for 12 weeks, showed an affected growth rate, decreased spermatozoid count, as well as decreased testosterone levels during gestation, lactation or weaning (WHO/Europe, 2003). Evidence of increased susceptibility of the young animal was noted in a rat multi-generation reproduction study and rat developmental neurotoxicity study (USEPA, 2002).

The available genotoxicity data indicate that gamma-HCH has some genotoxic potential. Gamma-HCH has been shown to increase chromosome clastogeny in bone marrow cells in mice exposed to 1.6 mg per kg body weight per day by gavage for 7 days (ATSDR, 2005). Nevertheless, lindane is not classified as genotoxic by the European Union (WHO/Europe, 2003). DNA damage was observed in cultures of rat nasal and gastric mucosa cells, and human nasal mucosa cells exposed to gamma-HCH and induced unscheduled DNA synthesis in certain types of cells, like human peripheral lymphocytes (ATSDR, 2005).

The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans; it has also classified technical HCH and alpha-HCH as possible human carcinogens (ATSDR, 2005). The US EPA has recently reclassified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". USEPA has classified technical-grade HCH and alpha-HCH as probable human carcinogens while beta-HCH is a possible human carcinogen (ATSDR, 2005).

Carcinogenicity of lindane has been tested by oral administration in different experiments. Some studies have shown no significant increases in endocrine, thyroid, pituitary, adrenal gland, liver, or ovary tumors in rats fed 10.8–33 mg/kg/day in the diet for 80 weeks, or 0.07–32 mg gamma-HCH/kg/day in the diet for 104 weeks, but poor survival rates limited the significance of such results (WHO/Europe, 2003). While other studies have reported hepatocellular carcinomas in mice exposed to 13.6–27.2 mg/kg/day in the diet for 80 or 104 weeks, and in mice exposed to 27.2 mg/kg/day in the diet for 96 weeks, these results were obtained in a strain of mouse that has a dominant mutation resulting in an increased susceptibility to formation of strain-specific neoplasms.

Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds and decreased body weight gain in mammals, with some effects indicative of endocrine disruption. Acute aquatic toxicity data on lindane indicate that it is highly toxic to both freshwater fish (LC_{50} ranges of 1.7 to 131 ppb) and aquatic invertebrates (LC_{50} ranges of 10.0 to 520 ppb). Chronic aquatic toxicity data for freshwater organisms show reduction in larval growth in freshwater fish at a NOAEC of 2.9 µg/l, and decreased reproduction in aquatic invertebrates at a NOAEC of 54 µg/l (CEC, 2005 and USEPA, 2006).

Lindane produced statistically significant sex ratio effects (71% males) in frogs at a level of 0.1 ppb and estrogenic activity as well as altered sperm responsiveness to progesterone and induced expression of vitellogenin and estrogen receptors in *in vitro* tests (USEPA, 2006). Reproductive and population effects were found at a LOAEL of 13.5 µg/l lindane in invertebrate in a 35 day study. Lindane at 100 ppm and 25 ppm caused reduced hatchability in both laying hens and Japanese quails, respectively (USEPA, 2006).

In 2002, USEPA published a dietary risk assessment for indigenous people in the Arctic for lindane. This dietary risk assessment is based on a number of hazard and exposure assumptions, and estimates risk to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The total dietary intakes for adults ranged from 0.000055 to 0.00071 mg/kg/day. For non-cancer effects, the Level of Concern was (LOC) =0.0016 mg/kg/day. The dietary risks for lindane did not exceed the LOC (USEPA, 2002).

Although the decision to include lindane in the Stockholm Convention would be based on the gamma isomer alone, the POPRC agreed that discussions could include the alpha and beta isomers. Therefore, information from a 2006 USEPA risk assessment on the alpha and beta isomers is included below.

In February 2006, USEPA published for public comment a risk assessment that discussed risks from lindane and the alpha- and beta-HCH isomers, by-products of the lindane manufacturing process (USEPA, 2006). Total dietary intakes were estimated for adults and children and ranged from 0.00057 to 0.051 mg/kg/day for alpha-HCH, and from 0.00037 to 0.01 mg/kg/day for beta-HCH. These dietary intakes were compared to USEPA's chronic level of concern (LOC). For non-cancer effects, the LOC is cRfD=0.00006 mg/kg/day for beta-HCH and a cRfD=0.001 mg/kg/day for alpha-HCH, based on the dose at which USEPA has concluded will result in no unreasonable adverse health effects. The cancer LOC is when the estimated upper bound cancer risk exceeds one in one million. The dietary risk assessment indicates that the chronic and cancer dietary risk estimates for alpha- and beta-HCH are above the USEPA levels of concern (LOC) for these Arctic populations based on high-end dietary intake estimates.

3.   Synthesis of information

Lindane has been shown to be neurotoxic, hepatotoxic, immunotoxic and to have reproductive effects in laboratory animals. Human acute intoxication data show that lindane can cause severe neurological effects, and chronic data suggest possible haematological effects. The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans

(ATSDR, 2005). The US EPA classified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential".

Human exposure to lindane, particularly in pregnant women and children, is a concern heightened by the ongoing presence of HCH isomers, including lindane, in human tissues and breast milk. Direct exposure from the use of pharmaceutical products for scabies and lice treatment should be of concern. Exposure from food sources is possibly of concern for high animal lipid content diets and subsistence diets of particular ethnic groups (USEPA, 2006 and CEC, 2005). Occupational exposure at manufacturing facilities should be of concern, because lindane production implies worker exposure to other HCH isomers as well, for example the alpha isomer is considered to be a probable human carcinogen (USEPA, 2006).

Lindane is very prevalent in the marine environment and soils, with higher concentrations often found in colder regions. The atmospheric long range transport potential of lindane has been demonstrated for the European Region (WHO/Europe, 2003).

Although current production of lindane seems to be declining with only a few producing countries remaining, the inefficient production process used to manufacture this insecticide over the years has been a world wide contamination problem which has left, and might still be leaving behind, an enormous legacy of contaminating waste products (IHPA, 2006).

The evaluation of laboratory experimental data of lindane would suggest a lower potential of bioaccumulation and biomagnification than that expected for other organochlorine pesticides. In fact, lindane should be considered a border case in terms of its potential for bioaccumulation. Fortunately, there is a large amount of monitoring data on biota allowing a real estimation of the risk profile of lindane in comparison with other organochlorine pesticides. The information provided by this huge amount of real field data is conclusive: lindane concentrations in biota samples collected far away from use areas is similar to that observed for other organochlorine pesticides, confirming the concern for persistence, bioaccumulation and long-range transport.

As the toxicity of lindane is also similar or even higher than that observed for other organochlorine pesticides, it should be considered that the concern related to the POP characteristics of lindane is equivalent to that observed for other chemicals already included in the Stockholm Convention. For example, Weisbrod et al., (2000) found lindane levels in pilot whales similar or just slightly lower than those found for aldrin, endrin, heptachlor or mirex. Also Sørmo et al. (2003) and Kannan et al. (2004) found equivalent levels for the sum of HCHs and for the sum of chlordanes in gray seal and sea otters respectively.

4.   Concluding statement

Lindane has been the subject of numerous risk assessment reports by different agencies, diverse country regulations and international initiatives, indicating the general concern raised by this organochlorine compound and indicating global action has already been undertaken.

The information provided in the present document, as well as the information contained in the numerous risk assessment reports published on lindane, indicate that lindane is persistent, bioccumulative and toxic, and is found in environmental samples all over the world as well as in human blood, human breast milk and human adipose tissue in different studied populations, especially impacting Arctic communities that depend on subsistence foods. These findings indicate

that lindane is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

Acknowledgements

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